



Fig.1.

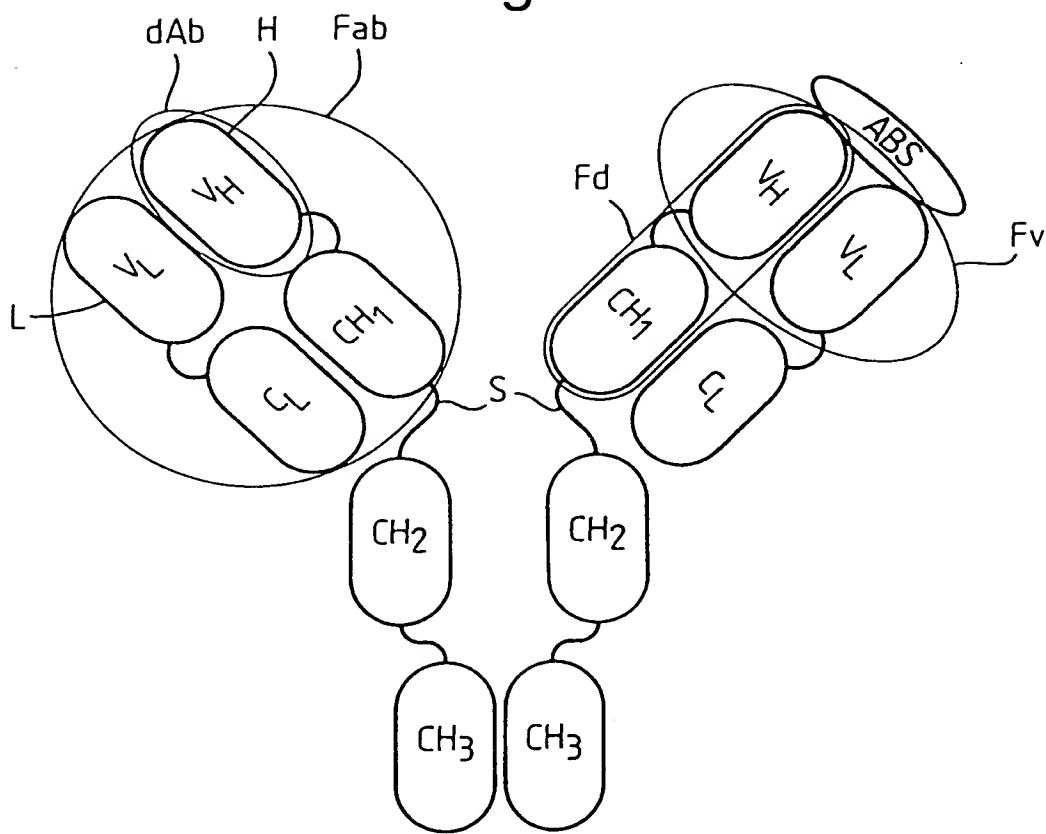




Fig.2a

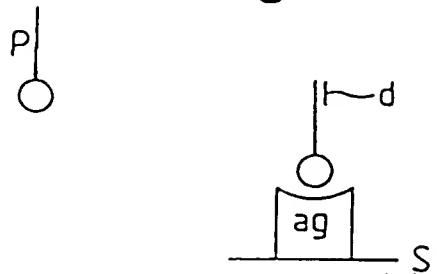


Fig.2b

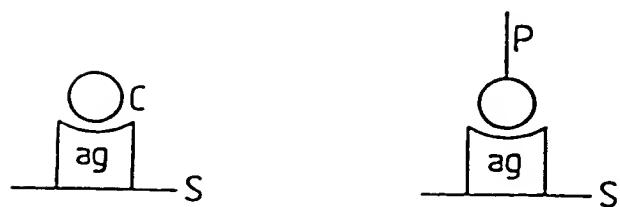
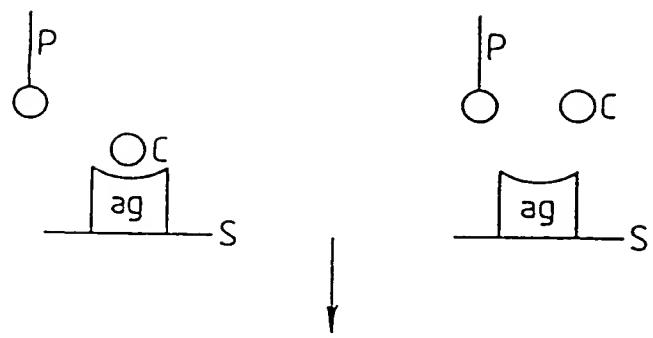
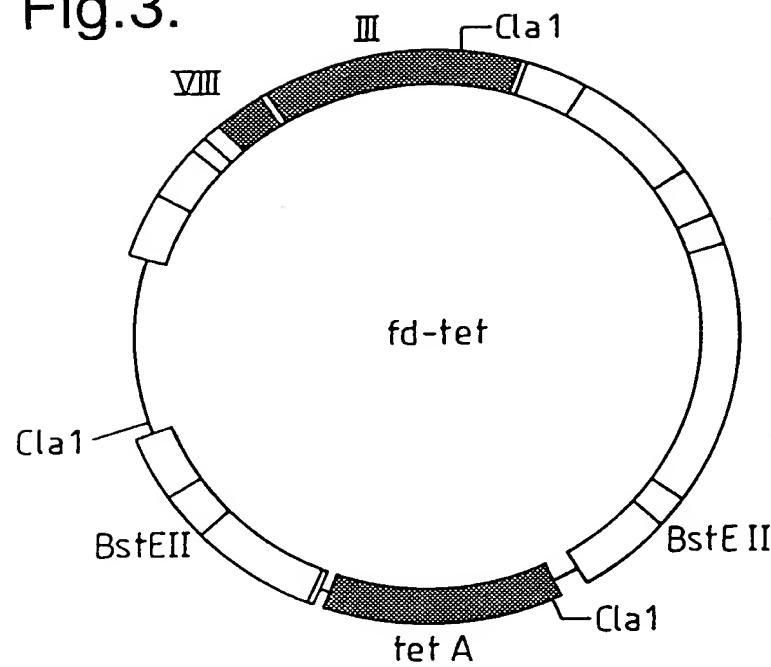




Fig.3.



fd - tet

▼

cleave with BstEII

▼

fill in with Klenow

▼

re-ligate

!

FDT6 Bst

▼

in vitro mutagenesis (oligo 1)

!

FDTPs/Bs

▼

in vitro mutagenesis (oligo 2)

!

FDTPs/Xh

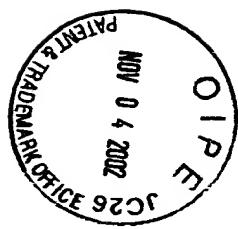


Fig. 4 a

Oligo 1	(1653) ACA ACT TTC AAC AGT TGA GGA GAC GGT GAC CGT AAG CTT CTG CAG TTG GAC CTG AGC	(SEQ ID NO. 177)
Oligo 2	(1653) ACA ACT TTC AAC AGT TTC CCG TTT GAT CTC GAG CTC CTG CAG TTG GAC CTG	(SEQ ID NO. 178)
Oligo 3	(1704) GTC GTC TTT CCA GAC GTT AGT	(SEQ ID NO. 179)

GENE III

Fig. 4 b

SIGNAL
CLEAVAGE SITE

(1624)
A TCT CAC TCC GCT

(1650)
GAA ACT GTT GAA AGT (SEQ ID NO. 180)

Q V Q L Q (SEQ ID NO. 1) V T V S S (SEQ ID NO. 2)

B TCT CAC TCC GCT CAG GTC CAA CTG CAG AAG CTT ACG GTC ACC GTC TCC TCA ACT GTT GAA AGT (SEQ ID NO. 181)

PstI BstEII

Q V Q L Q (SEQ ID NO. 1) L E I K R (SEQ ID NO. 3)

C TCT CAC TCC GCT CAG GTC CAA CTG CAG GAG CTC GAG ATC AAA CGG GAA ACT GTT GAA AGT (SEQ ID NO. 182)

PstI XbaI

REV 04 2002

TRADEMARK OFFICE
JC26

Fig.5a

rbs

M K Y L L P T A A

GCATGCAAATTCTATTTCAGGAGACAGTCATAATGAAATACCTATTGCCTACGGCAGCC

10 20 30 40 50 60

SphI

PelB leader

A G L L L A A O P A M A Q V Q L Q E S
GCTGGATTGTATTACTCGTGCCAACAGCGATGGCCAGGTGCAGCTGCAGGAGTC

70 80 90 100 110 120

PstI

G P G L V A P S Q S L S I T C T V S G F
GGACCTGGCTGGTGGCGCCCTCACAGAGCCTGTCCATCACATGCACCGTCTCAGGGTTC
130 140 150 160 170 180

S L T G Y G V N W V R Q P P G K G L E W
TCA'TTAACCGGCTATGGTGTAAACTGGGTGGCCAGCCTCCAGGAAGGGCTGGAGTGG
190 200 210 220 230 240

VHD1.3

L G M I W G D G N T D Y N S A L K S R L
CTGGGAATGATTGGGTGATGGAAACACAGACTATAATTAGCTCTCAAATCCAGACTG
250 260 270 280 290 300

S I S K D N S K S Q V F L K M N S L H T
AGCATCAGCAAGGACAACCTCAAGAGCCAAGTTCTAAAAATGAACAGTCTGCACACT
310 320 330 340 350 360

D D T A R Y Y C A R E R D Y R L D Y W G
GATGACACAGCCAGGTACTACTGTGCCAGAGAGAGATTATAGGCTTGACTACTGGGC
370 380 390 400 410 420

Linker Peptide

Q G T T V T V S S G G G G S G G G G S G
CAAGGCACCACGGTCACCGTCTCCTCAggtgaggcggttcaggcggaggtggctcggc
430 440 450 460 470 480

BstEII

G G G S D I E L T Q S P A S L S A S V G
ggtggcgatcgGACATGAGCTCACTCAGTCTCCAGCCTCCCTCTGCGTCTGTGGGA
490 500 510 520 530 540

SacI



Fig.5 b

E T V T I T C R A S G N I H N Y L A W Y
GAAACTGTCAACCACATCACATGTGGAGCAAGTGGGAATATTTCACAATTATTTAGCATGGTAT
550 560 570 580 590 600

Q Q K Q G K S P Q L L V Y Y T T T L A D
CAGCAGAAACAGGGAAAATCTCCTCAGCTCCTGGCTATTATAACAACAACTTAGCAGAT
610 620 630 640 650 660

VKD1.3

G V P S R F S G S G S G T Q Y S L K I N
GGTGTGCCATCAAGGTTCAAGTGGCAGTGGATCAGGAACACAATATTCTCTCAAGATCAAC
670 680 690 700 710 720

S L Q P E D F G S Y Y C Q H F W S T P R
AGCCTGCAACCTGAAGATTTGGGAGTTATTACTGTCAACATTTGGAGTACTCCTGG
730 740 750 760 770 780

Myc Tag (TAG1)

T F G G G T K L E I K R E O K L I S E E
ACGTTGGTGGAGGGACCAAGCTGGAGATCAAACGGAACAAAAACTCATCTCAGAAGAG
790 800 810 820 830 840

XbaI

D L N * * (SEQ ID NO. 183)

GATCTGAATTATAATGATCAAACGGTAATAAGGATCCAGCTGGATTTC (SEQ ID NO. 184)
850 860 870 880

EcoRI



Fig.6.

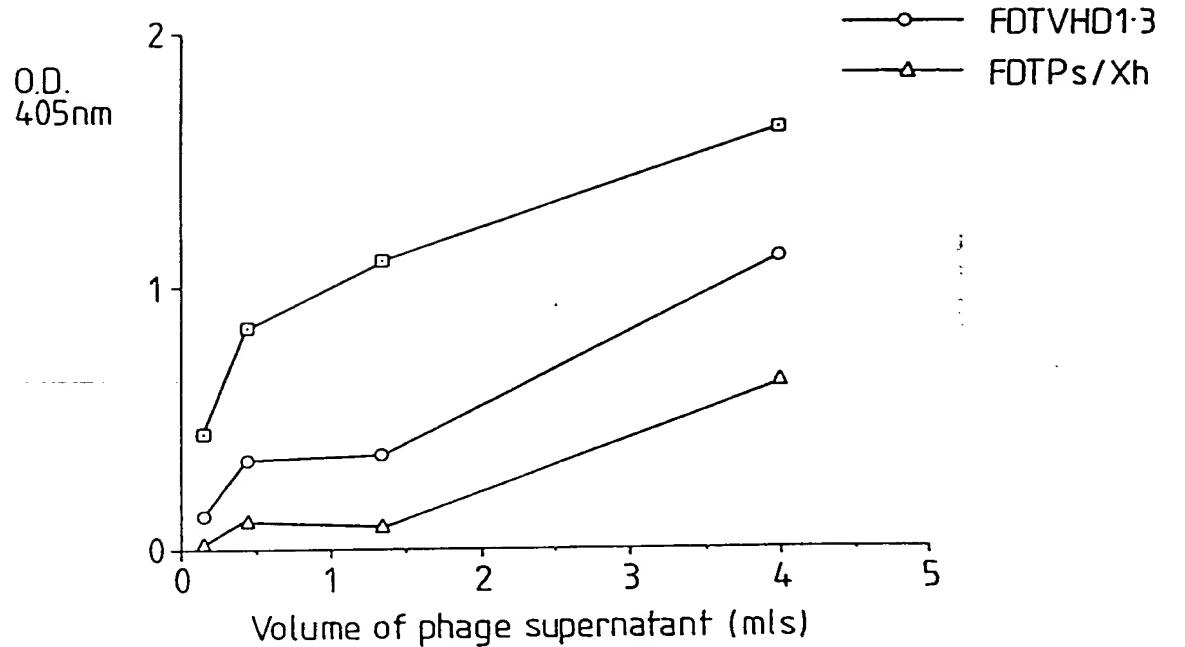


Fig.7.

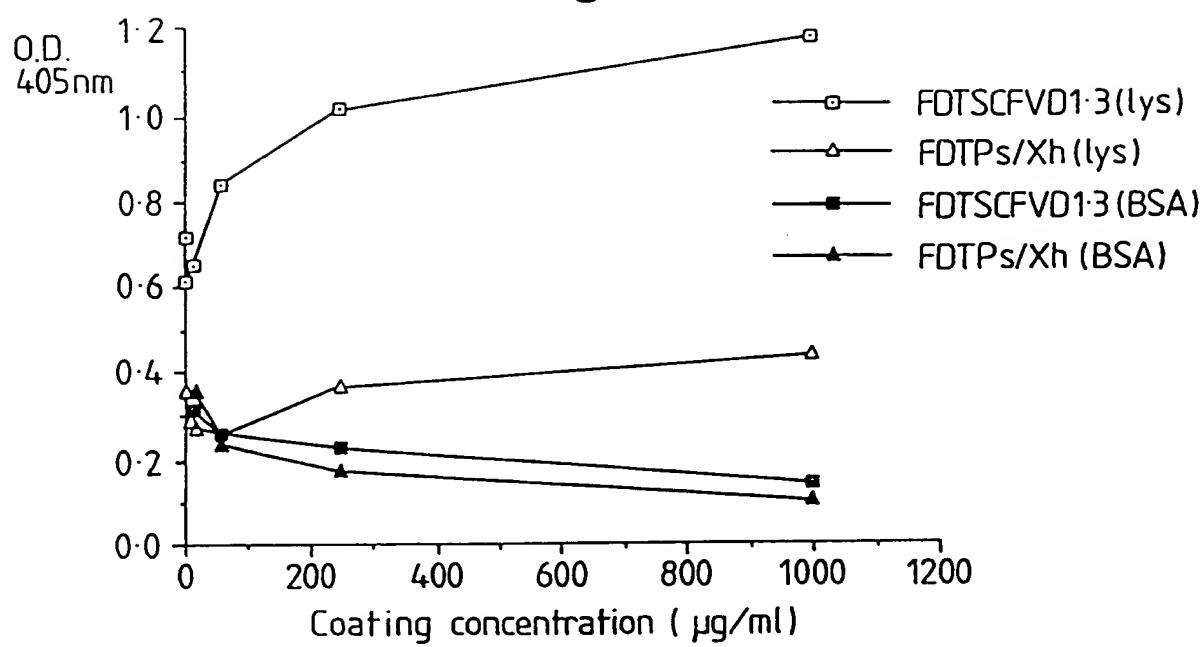




Fig.8.

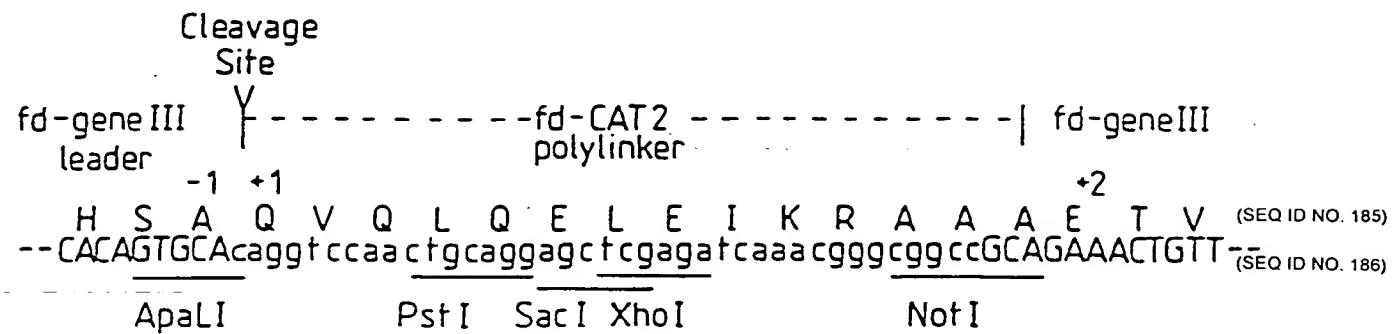


Fig.9.

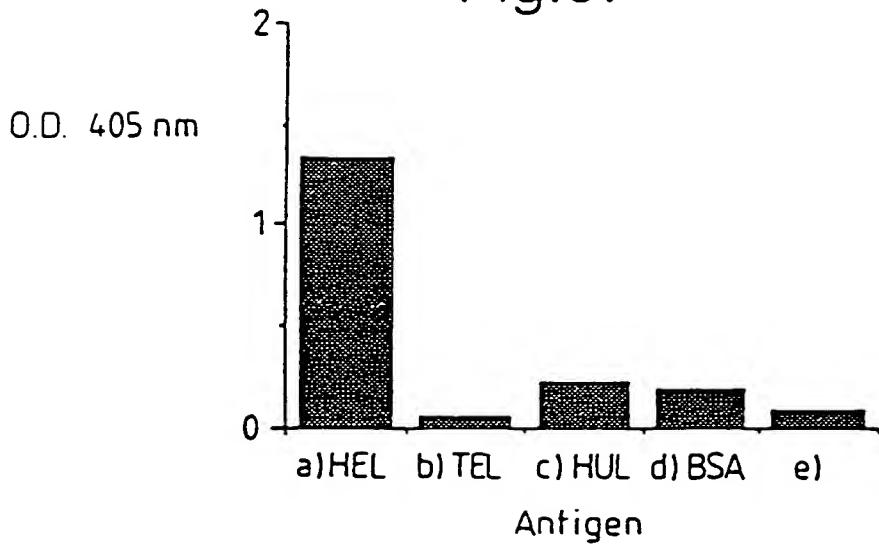




Fig.10a

M K Y L L P T A A
GCATGCAAATTCTATTCAAGGAGACAGTCATAATGAAATACCTATTGCTAACGGCAGCC
10 20 30 40 50 60

A G L L L L A A Q P A M A Q V Q L Q E S
GCTGGATTGTATTACTCGCTGCCAACCAACCAGCGATGCCGTTGCCAGCTGCAGGAGTCA
70 80 90 100 110 120

G P G L V A P S Q S L S I T C T V S G F
GGACCTGGCTGGTGGGCCCTCACAGAGCCTGTCATCACATGCACCGTCTCAGGGTTC
130 140 150 160 170 180

S L T G Y G V N W V R Q P P G K G L E W
TCATTAACGGCTATGGTGTAAACTGGGTCTGGCAAGCTTCAAGAAAGGGTCTGGAGTGG
190 200 210 220 230 240

L G M I W G D G N T D Y N S A L K S R L
CTGGGAATGATTGGGGTGATGGAAACACAGACTATAATTAGCTCTCAAATCCAGACTG
250 260 270 280 290 300

S I S K D N S K S Q V F L K M N S L H T
AGCATCAGCAAGGACAACCTCCAAGAGCCAAGTTTCTAAAAATGAACAGTCTGCACACT
310 320 330 340 350 360

D D T A R Y Y C A R E R D Y R L D Y W G
GATGACACAGOCAGGTACTACTGTGCTAGAGAGAGAGATTATAGGCTTGACTACTGGGGC
370 380 390 400 410 420

Q G T T V T V S S A S T K G P S V F P L
CAAGGCACCAAGGTCAACGGCTCTGGCTAGCTTCAAGGGCCATGGCTTCCCCCTG
430 440 450 460 470 480

A P S S K S T S G G T A A L G C L V K D
GCAACCTCTCAAGAGCACCTCTGGGGCACAGGGGCGCTGGCTGCCIGGTCAAGGAC
490 500 510 520 530 540



Fig.10b

Y F P E P V T V S W N S G A L T S G V H
TACTTCCCCGAAACGGTGACGGTGCGAAGCTCAGGCGCCCTGACCCAGGGGTGCCAC
550 560 570 580 590 600

T F P A V L Q S S G L Y S L S S V V T V
ACCTTCCCCGGCTGCTAACAGTOCTCAGGACTCTACTCCCTCAGCAGGGTGGTGACCGTG
610 620 630 640 650 660

P S S S L G T Q T Y I C N V N H K P S N
CCTCAGGAGCTGGGACCCAGACCTACATCIGCAACGTGAATCACAAAGCCAGCAAC
670 680 690 700 710 720

T K V D K K V E P K S S * * (SEQ ID NO. 187)
ACCAAGCTGAGATAAGAAAGTTGACCCAAATCTTCATAATAACCCGGAGCTTGATGCA
730 740 750 760 770 780

M K Y L L P T A A A A G L.
AATTCTATTCAAGGAGACAGTCATAATGAAATACTTATGCTAACGGCAGCGCTGGAT
790 800 810 820 830 840

L L L A A Q P A M A D I E L T Q S P A S
TGTTATTACTGGTGGCCAACCAGCGATGGCGACATGAGCTAACCGAGCTCAGGCT
850 860 870 880 890 900

L S A S V G E T V T I T C R A S G N I H
CCCTTCTGGCTCTGGGAGAACTGTCACCATCACATGTCAGGCAAGTGGGAATATTIC
910 920 930 940 950 960

N Y L A W Y Q Q K Q G K S P Q L L V Y Y
ACAATTATTACCACTGGTATCAGCAGAAACAGGGAAAATCTCCCTCAGCTCTGGCTATT
970 980 990 1000 1010 1020



Fig.10 c

T T T L A D G V P S R F S G S G S G T Q
 ATACAACAAACCTTAGCAGATGGTGTGOCATCAAGGTTCAGTGCCAGTGGATCAGGAACAC
 1030 1040 1050 1060 1070 1080

Y S L K I N S L Q P E D F G S Y Y C Q H
 AATATTCTCTCAAGATCAAACAGCTGGAGCTGAAGATTTGGGAGTTATTACTGTCAC
 1090 1100 1110 1120 1130 1140

F W S T P R T F G G G T K L E I K R T V
 ATTTTGGAGTACTCTGGACGTTCGGTGGAGGCCACCAAGCTGGAGATCAAACGGACTG
 1150 1160 1170 1180 1190 1200

A A P S V F I F P P S D E Q L K S G T A
 TGGCTGCACCATCTGCTTCATCTTCCCCGACATCTGATGAGCAGTTGAAATCTGGAACCTG
 1210 1220 1230 1240 1250 1260

S V V C L L N N F Y P R E A K V Q W K V
 CCTCTGGTGGCTGGCTGAATACTCTATCCCCAGAGGCCAAAGTACAGTGGAAAG
 1270 1280 1290 1300 1310 1320

D N A L Q S G N S Q E S V T E Q D S K D
 TGGATAACGCCCTCCAATGGGTAACCTCCAGGAGAGTGTACAGAGCAGGACAGCAAGG
 1330 1340 1350 1360 1370 1380

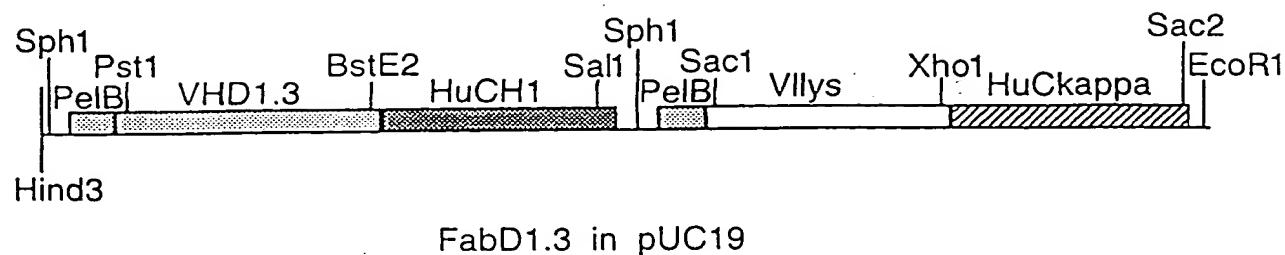
S T Y S L S S T L T L S K A D Y E K H K
 ACAGCACCTACAGCCTCAGCAGCACCCCTGAGCTGAGCAAASCAGACTACGAGAACACA
 1390 1400 1410 1420 1430 1440

V Y A C E V T H Q G L S S P V T K S F N
 AAGTCATGGCTGGAGTCACCCATCAGGCGCTGAGCTGGCGGTACAAAGAGCTTCA
 1450 1460 1470 1480 1490 1500

R G E S * * (SEQ ID NO. 188)
 ACGGGAGAGTCATAGTAAGAATT (SEQ ID NO. 189)
 1510 1520



Fig.10 d



FabD1.3 in pUC19

Fig.11.

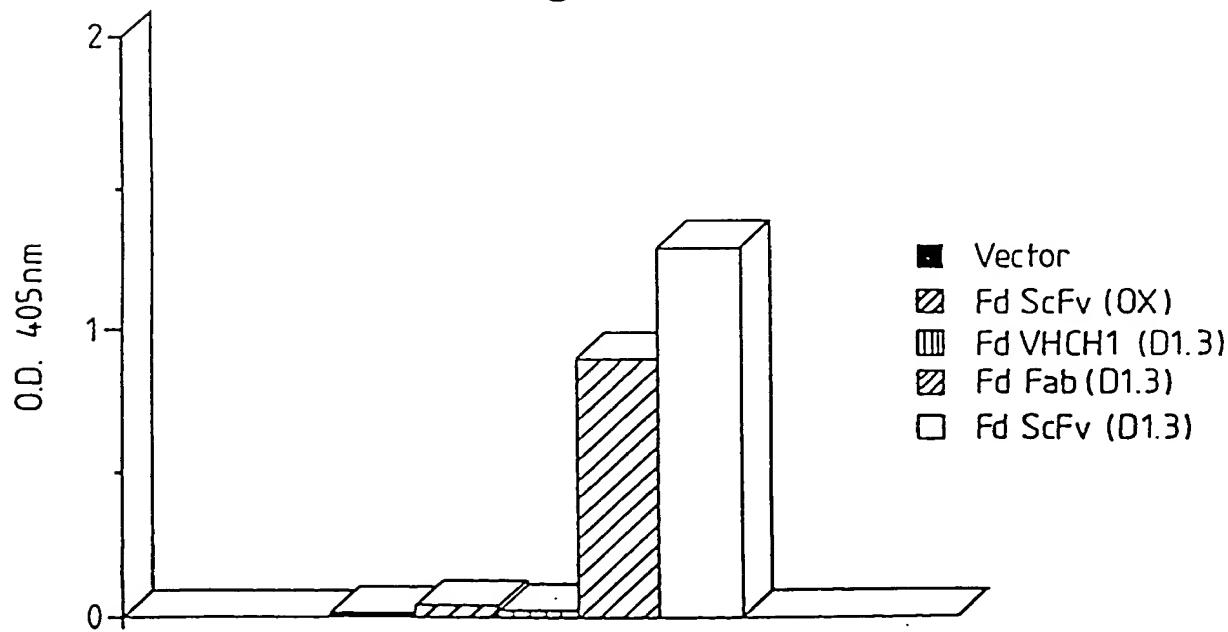




Fig.12a.

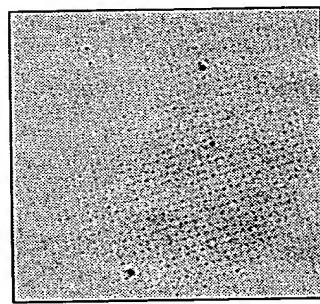


Fig.12b.

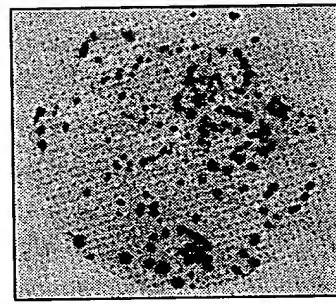




Fig. 13.

Q V Q L Q E S G G G L V Q P G G
 CAG GTG CAG CTG CAG GAG TCA GGA GGA GGC TTG GTA CAG CCT GGG GGT
PstI
 S L R L S C A T S G F T F S N Y
 TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC AGT AAT TAC
 Y M G W V R Q P P G K A L E W L
 TAC ATG GGC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG
 G S V R N K V N G Y T T E Y S A
 GGT TCT GTT AGA AAC AAA GTT AAT GGT TAC ACA ACA GAG TAC AGT GCA
 S V K G R F T I S R D N F Q S I
 TCT GTG AAG GGG CGG TTC ACC ATC TCC AGA GAT AAT TTC CAA AGC ATC
 L Y L Q I N T L R T E D S A T Y
 CTC TAT CTT CAA ATA AAC ACC CTG AGA ACT GAG GAC AGT GCC ACT TAT
 Y C A R G Y D Y G A W F A Y W G
 TAC TGT GCA AGA GGC TAT GAT TAC GGG GCC TGG TTT GCT TAC TGG GGC
 Q G T L V T V S S g g g g s g g g g s
 CAA GGG ACC CTG GTC ACC gtc tcc tca gg^tggaggcggtt^tcaggcggagg^tggctt^t
BstEII
 g g g g s d i E L T Q T P L S L P V
 ggcgtggcggtt^tcgac atc GAG CTC ACC CAA ACT CCA CTC TCC CTG CCT GTC
SacI
 S L G D Q A S I S C R S S Q S I
 AGT CTT GGA GAT CAA GCC TCC ATC TCT TGC AGA TCT AGT CAG AGC ATT
 V H S N G N T Y L E W Y L Q K P
 GTA CAT AGT AAT GGA AAC ACC TAT TTA GAA TGG TAC CTG CAG AAA CCA
PstI
 G Q S P K L L I Y K V S N R F S
 GGC CAG TCT CCA AAG CTC CTG ATC TAC AAA GTT TCC AAC CGA TTT TCT
 G V P D R F S G S G T D F T
 GGG GTC CCA GAC AGG TTC AGT GGC AGT GGA TCG GGG ACA GAT TTC ACA
 L K I S R V E A E D L G V Y Y C
 CTC AAG ATC AGC AGA GTG GAG GCT GAG GAT CTG GGA GTT TAT TAC TGC
 F Q G S H V P Y T F G G G T K L
 TTT CAA GGT TCA CAT GTT CCG TAC ACG TTC GGA GGG GGG ACC AAG CTC
 E I K R
GAG ATC AAA CGG (SEQ ID NO. 190)
 XbaI (SEQ ID NO. 191)



Fig.14.

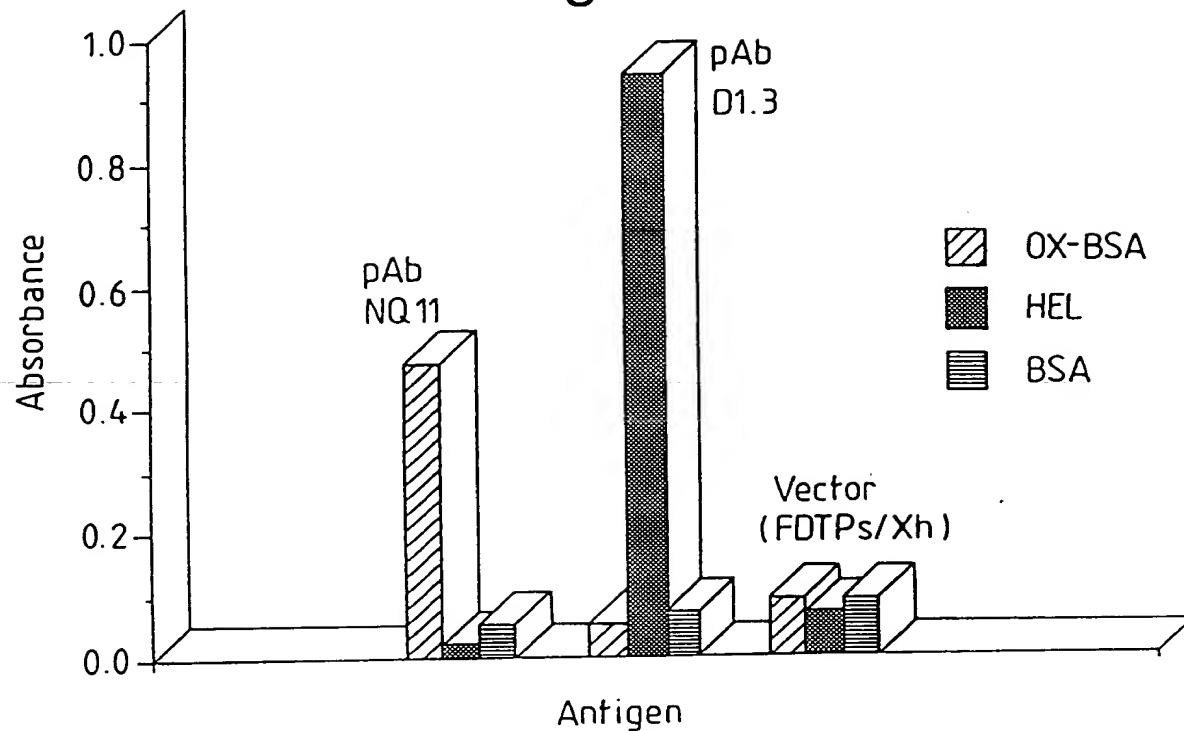


Fig.15.

5' END
 TCT CAC AGT GCA CAA ACT GTT GAA CGG ACA CCA GAA ATG CCT GTT CTG (SEQ ID NO:192)
 ApaL1 (SEQ ID NO:193)

3' END
 K A A L G L K (SEQ ID NO:194)
 AAA GCC GCT CTG GGG CTG AAA GCG GCC GCA GAA ACT GTT GAA AGT etc. (SEQ ID NO:195)
 Not I



Fig.16a

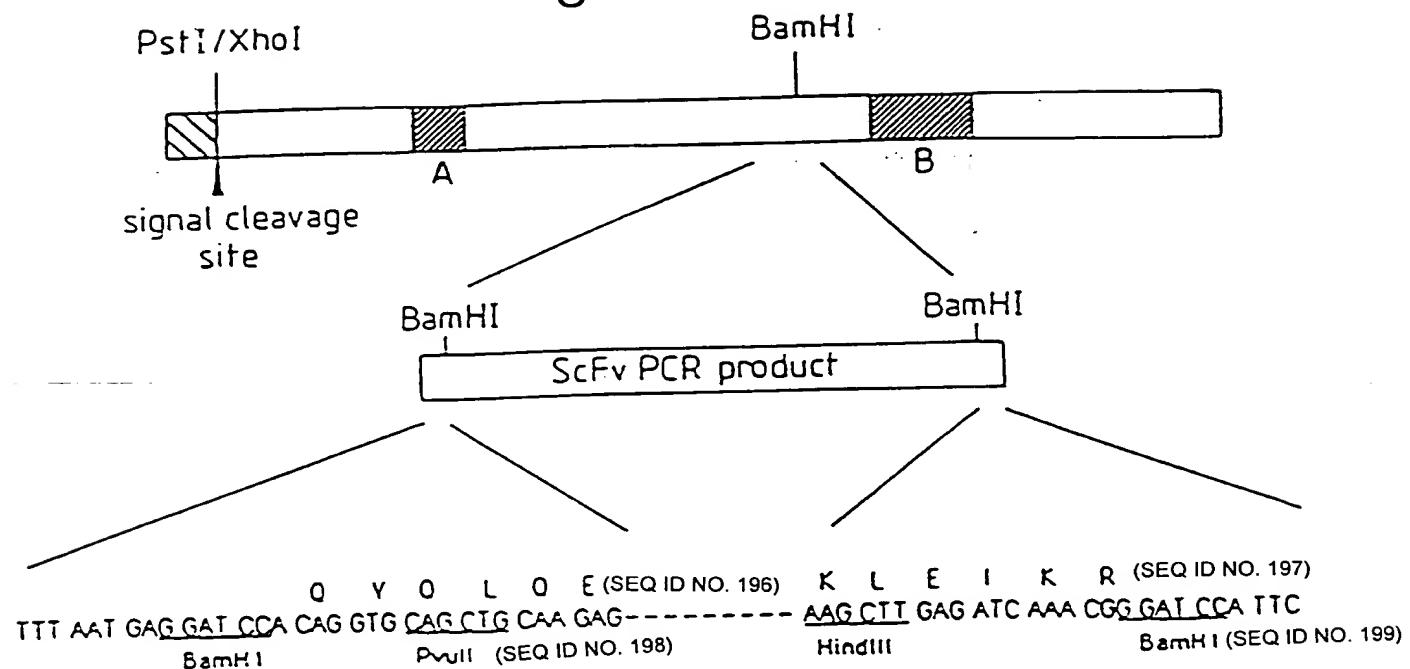


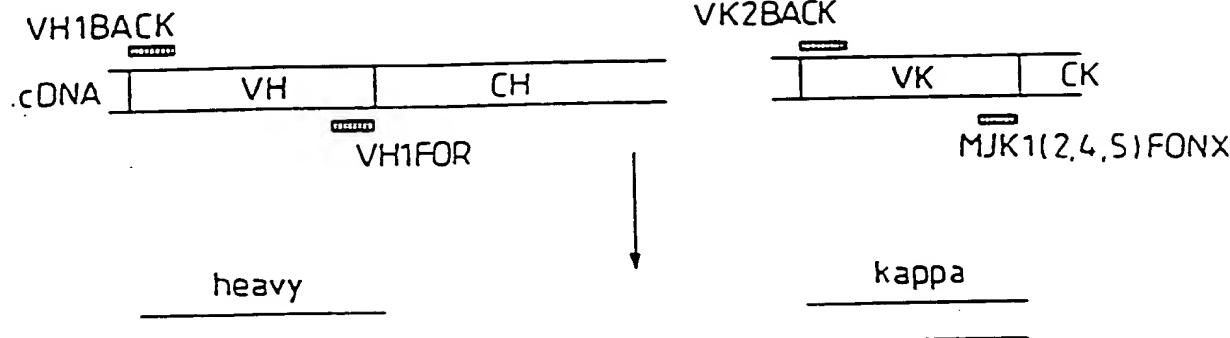
Fig.16b

A	(1834) 5' GAG GGT GGT GGC TCT	(SEQ ID NO. 200)
	- - - C - -	(SEQ ID NO. 201)
	- - - C - -	(SEQ ID NO. 202)
	- - - C - ACT 3' (1839)	(SEQ ID NO. 203)
B	(2284) 5' - GGC GGC GGC TCT	(SEQ ID NO. 204)
	- GGT GGT GGT -	(SEQ ID NO. 205)
	- - GGC GGC -	(SEQ ID NO. 206)
GAG	- - GGC -	(SEQ ID NO. 207)
	- - GGT -	(SEQ ID NO. 208)
	- - GGC -	(SEQ ID NO. 209)
	- - GGT -	(SEQ ID NO. 210)
	- - GGC - 3' (2379)	(SEQ ID NO. 211)
Reverse complement of mutagenic oligo G3Bamlink		5' GAG GGT GGC GGA TCC (SEQ ID NO. 212)
		T GAG GGT GGC GG 3' (SEQ ID NO. 213)

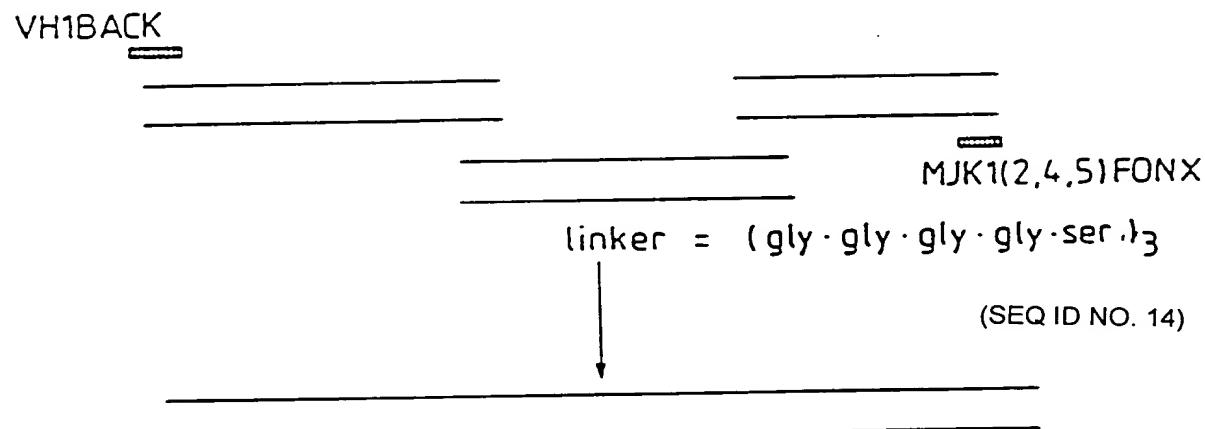


Fig. 17.

1) PRIMARY PCR



2) ASSEMBLY PCR



3) ADDING RESTRICTION SITES

VHBKA PA10

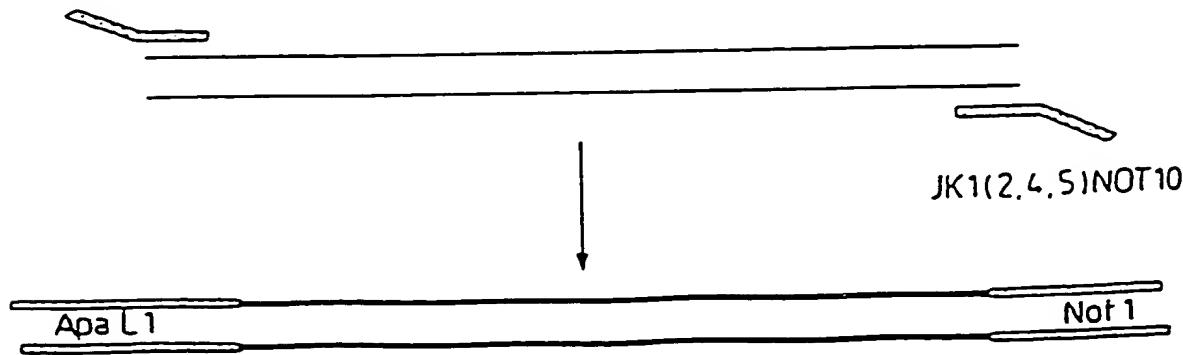




Fig.18.

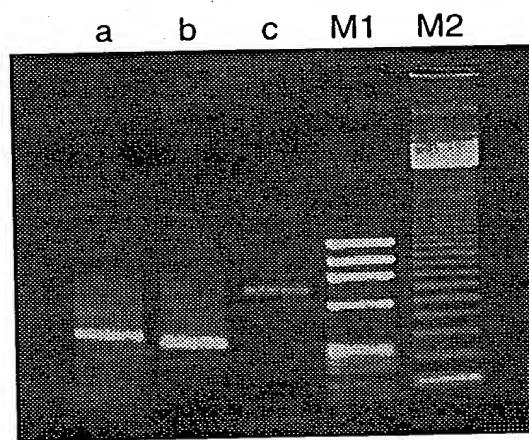




Fig.19.

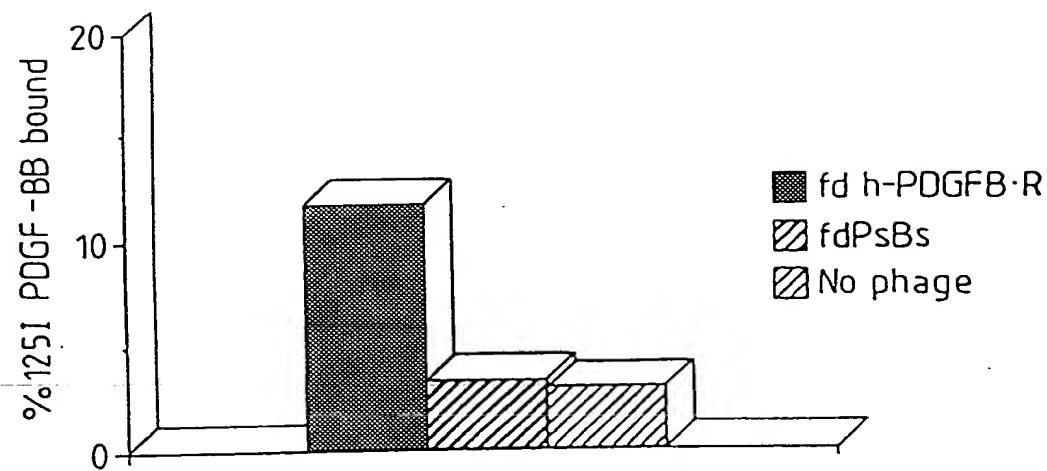


Fig.20.

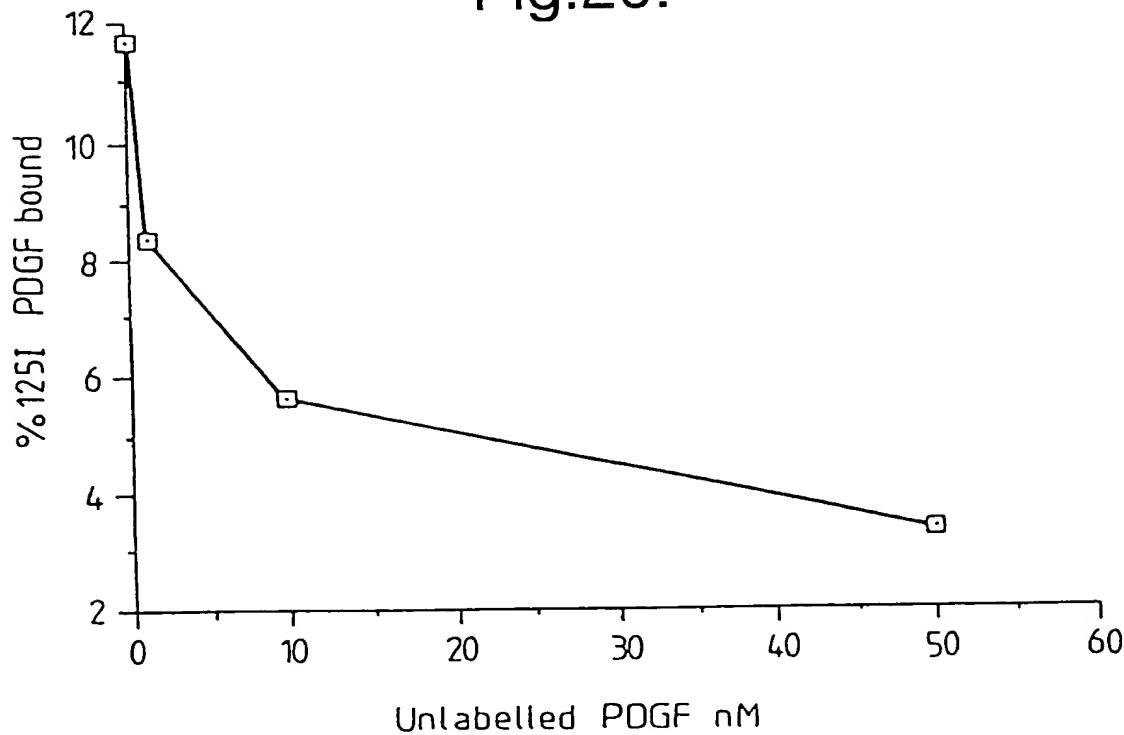




Fig.21.

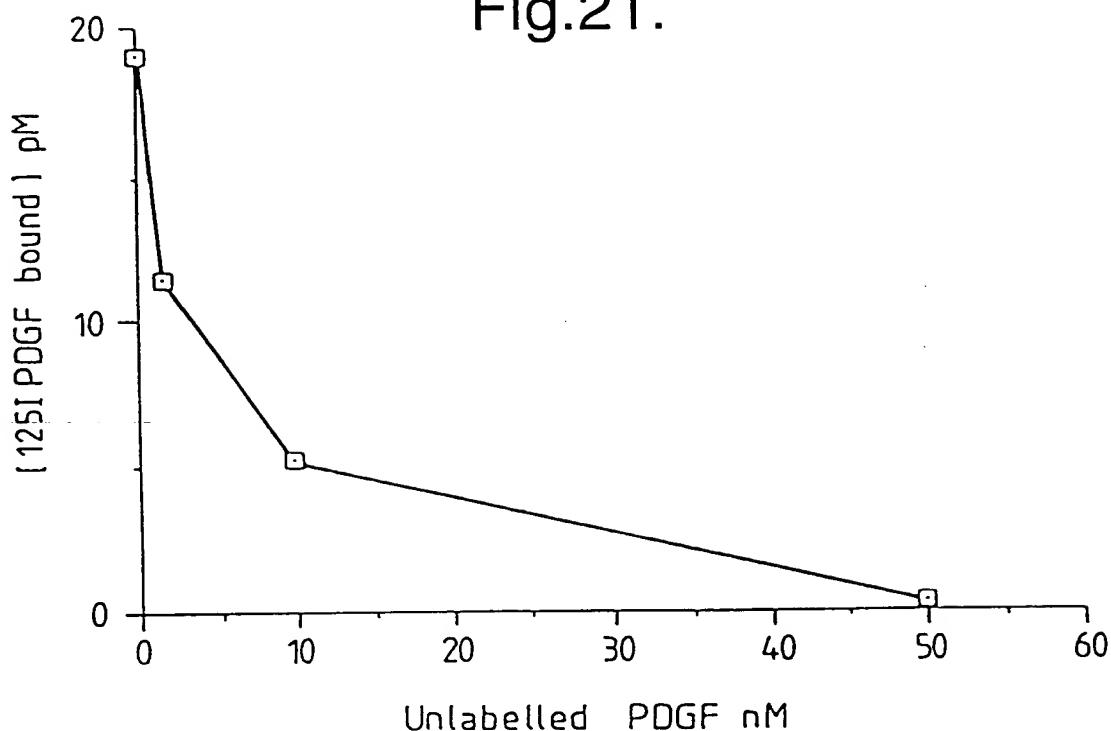


Fig.22.

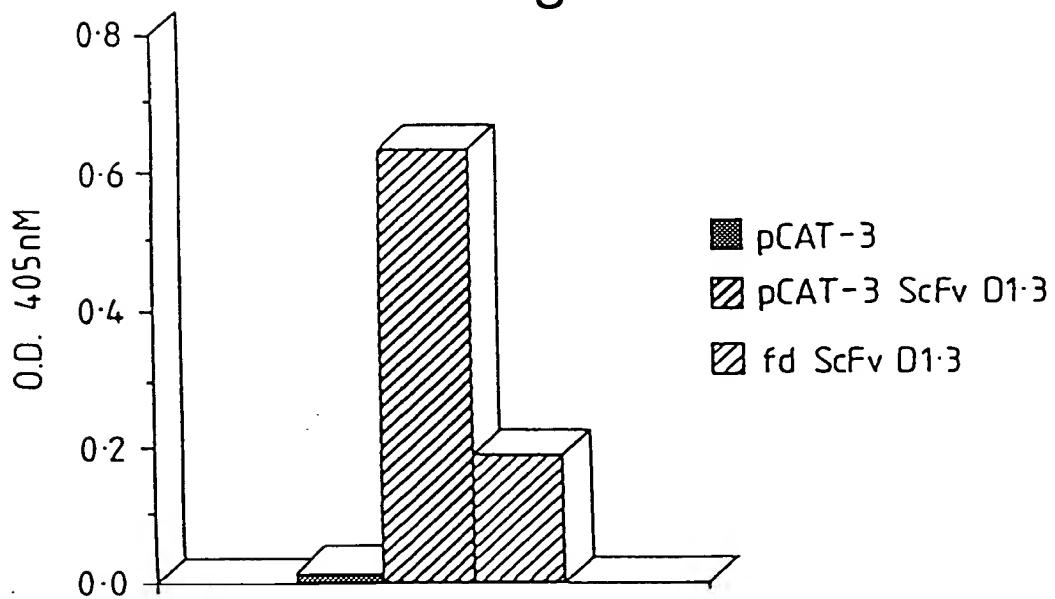




Fig.23a

d
M

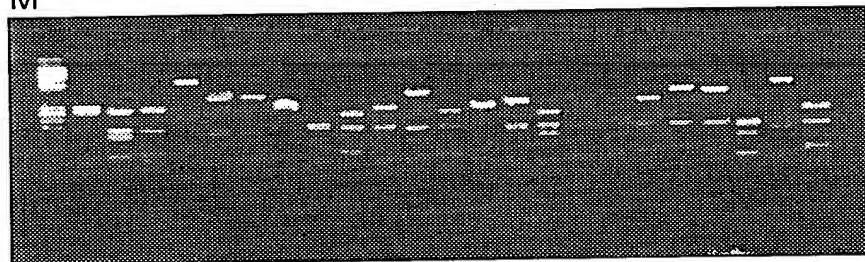
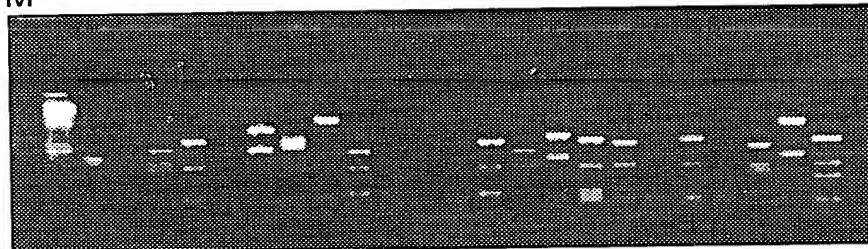


Fig.23 b

M





VH sequences

Fig.24a

from combinatorial library:

A QVQLQSGAEELAKPGASVYHSCKASGTTT
B QVQLQSGAEELAKPGASVYHSCKASGTTT
C QVQLQSGAEELAKPGASVYHSCKASGTTT
D QVQLQSGAEELAKPGASVYHSCKASGTTT
E QVQLQSGAEELAKPGASVYHSCKASGTTT
F QVQLQSGAEELAKPGASVYHSCKASGTTT
G QVQLQSGAEELAKPGASVYHSCKASGTTT
H QVQLQSGAEELAKPGASVYHSCKASGTTT

	CD11	CD12	CD13	CD14
A	SYTPII	WVKQRPQCGCLEMIG	YINPSEGCTHYNQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
B	ADMPII	WVKQRPQCGCLEMIG	YINPSTCYTEYHQKFKD	KATLTADKESSTA YMQLSSLTSESDSAVYTCAR
C	SYPPII	WVKQRPQCGGLEMIG	YINPTHQCTKHEKFKD	KATLTADKESSTA YMELSELTSSESDSAVYTCAR
D	GIFPN	WVKQSGICKSLEMIG	RINPTNGOFTYHQKFKD	KATLTADKESSTA YMELSELTSSESDSAVYTCAR
E	SYVHII	WVKQPPCKGLLEMIG	RUSISKONISQVFLKHKISIQTUDTAHYTCAR	RUSISKONISQVFLKHKISIQTUDTAHYTCAR
F	STLHII	WVKQRPQCGQKLMIG	YINPSTCYTEYHQKFKD	KATLTADKESSTA YHOLBLTSSESDSAVYTCAR
G	RILHII	WVKQBPQCGKSLRMIG	YINPSTCYTEYHQKFKD	ENTLTADKESSTA YHQLBLSESDSAVYTCAR
H	RIMHII	WVKQBGKGKSLRMIG	YINPSTCYTEYHQKFKD	KATLTADKESSTA YHQLBLSESDSAVYTCAR

in hierarchical library VH-rep x Vx-d:

I QVQLQSGAEELAKPGASVYHSCKASGTTT
J QVQLQSGAEELAKPGASVYHSCKASGTTT
K QVQLQSGAEELAKPGASVYHSCKASGTTT
L QVQLQSGAEELAKPGASVYHSCKASGTTT
M QVQLQSGAEELAKPGASVYHSCKASGTTT
N QVQLQSGAEELAKPGASVYHSCKASGTTT
O QVQLQSGAEELAKPGASVYHSCKASGTTT
P QVQLQSGAEELAKPGASVYHSCKASGTTT
Q QVQLQSGAEELAKPGASVYHSCKASGTTT
R QVQLQSGAEELAKPGASVYHSCKASGTTT
S QVQLQSGAEELAKPGASVYHSCKASGTTT
T QVQLQSGAEELAKPGASVYHSCKASGTTT
U QVQLQSGAEELAKPGASVYHSCKASGTTT
V QVQLQSGAEELAKPGASVYHSCKASGTTT
W QVQLQSGAEELAKPGASVYHSCKASGTTT

	CD11	CD12	CD13	CD14
I	SYTPII	WVKQSGSOKSLEMIG	VISTYNCHTMQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
J	RTTPII	WVKQRPQCGCLEMIG	YINPBCYCITYHQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
K	ROMHII	WVKQRPQCGCLEMIG	YINPSTCYTEYHQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
L	NTLHII	WVKQRPQCGGLEMIG	YINPSTCYTEYHQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
M	NTRHII	WVKQRPQCGGLEMIG	YINPSTCYTEYHQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
N	ETRAHII	WVKQRPQCGGLEMIG	YINPSSGTYTHNQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
O	SHUHII	WVKQRPQCGCLEMIG	YINPRTCYTEYHQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
P	SYTHII	WVKQRPQCGCLEMIG	YINPSTCYTEYHQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
Q	STTHII	WVKQRPQCGCLEMIG	YINPSTCYTEYHQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
R	STRHII	WVKQRPQCGGLEMIG	YINPSTCYTEYHQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR
S	RDHHII	WVKQRPQCGGLEMIG	YINPSTCYTEYHQKFKD	KATLTADKESSTA THQLSSLTSESDSAVYTCAR



Fig. 24b

V_K sequences

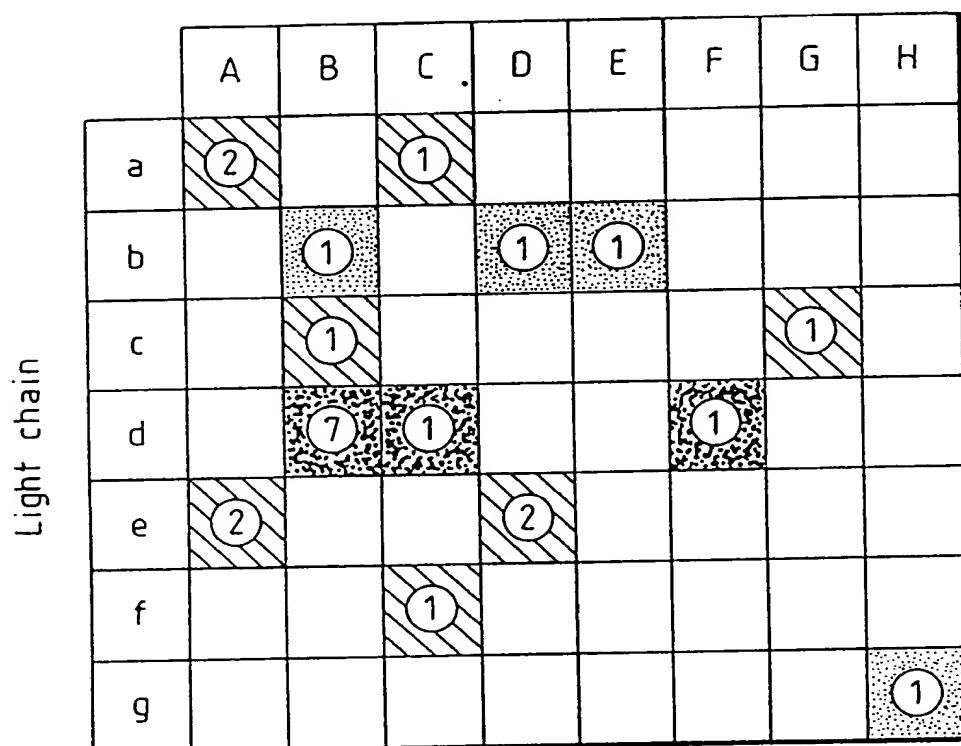
combinatorial library

From hierarchical library via B x Vx·rep:

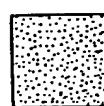


Fig.25.

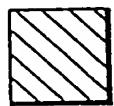
HEAVY CHAIN



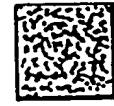
OD_{405nm} in ELISA



0.2 - 0.9



0.9 - 2.0



>2.0



Fig.26(a).

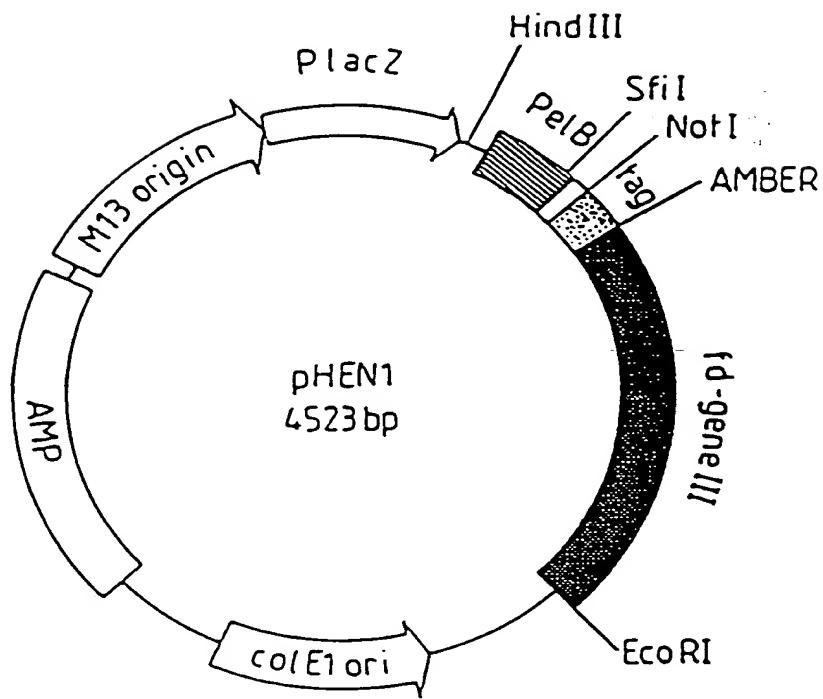


Fig.26(b).

PelB leader ————— + ————— pHEN1 polylinker —————

-1 +1

L L A A Q P A M A Q V Q L Q V D L E I K R

--TTACTCGCGGCCAGccatggcccaaggctgcagctgcaggcgtcacctcgagatcaaacgg

SfiI NcoI PstI SalI XbaI

— — — — — | — — — — c-myc tag — — — — — | — — — — — fd-gene III — — — — —

A A A E Q K L I S E E D L N G A A (5) T V E (SEQ ID NO. 25e)
gcggccgcAGAACAAAAACTCATCTCAGAAGAGGATCTGAATGGGGCCGCATAGACTGTTGAA (SEQ ID NO. 26e)

NotI

amber



Fig.27.

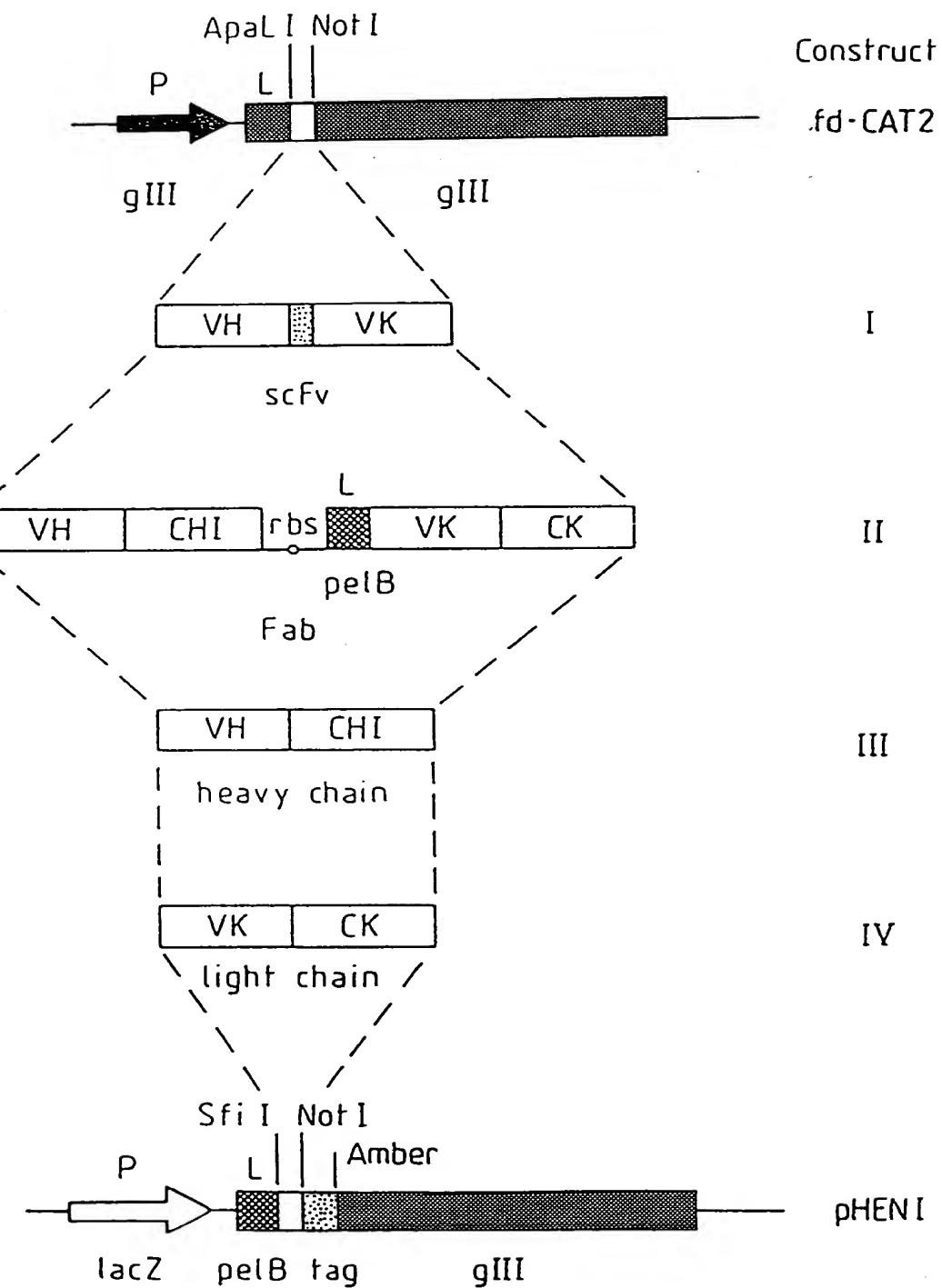
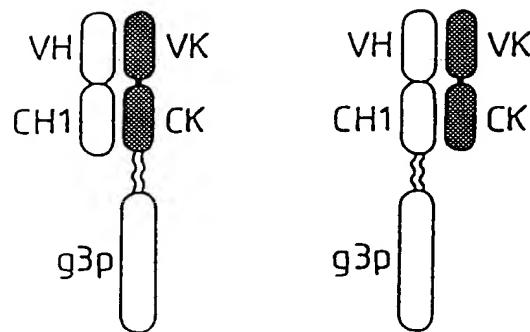




Fig.28.

Fab



VH VK

g3p

scFv



Fig.29.

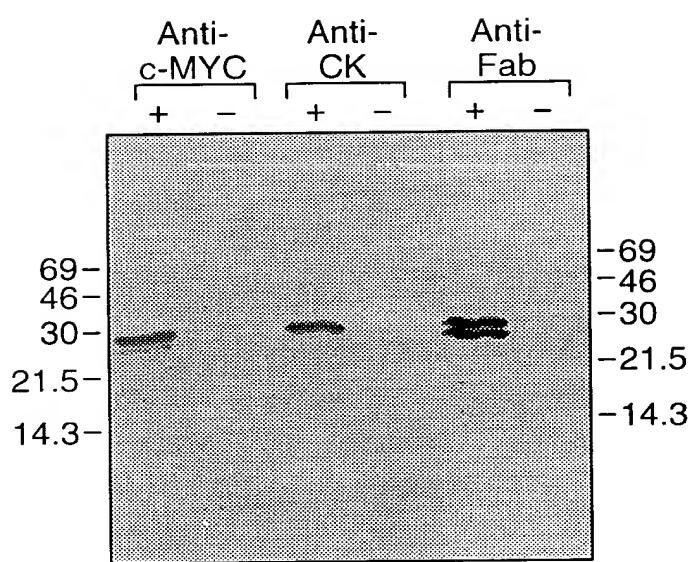




Fig.30.

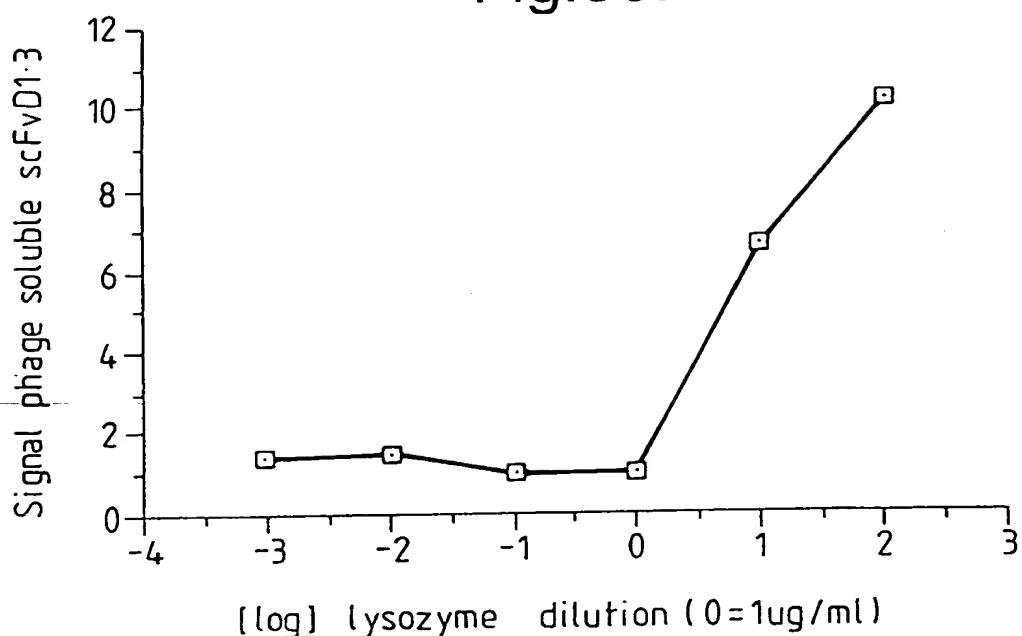


Fig.31.

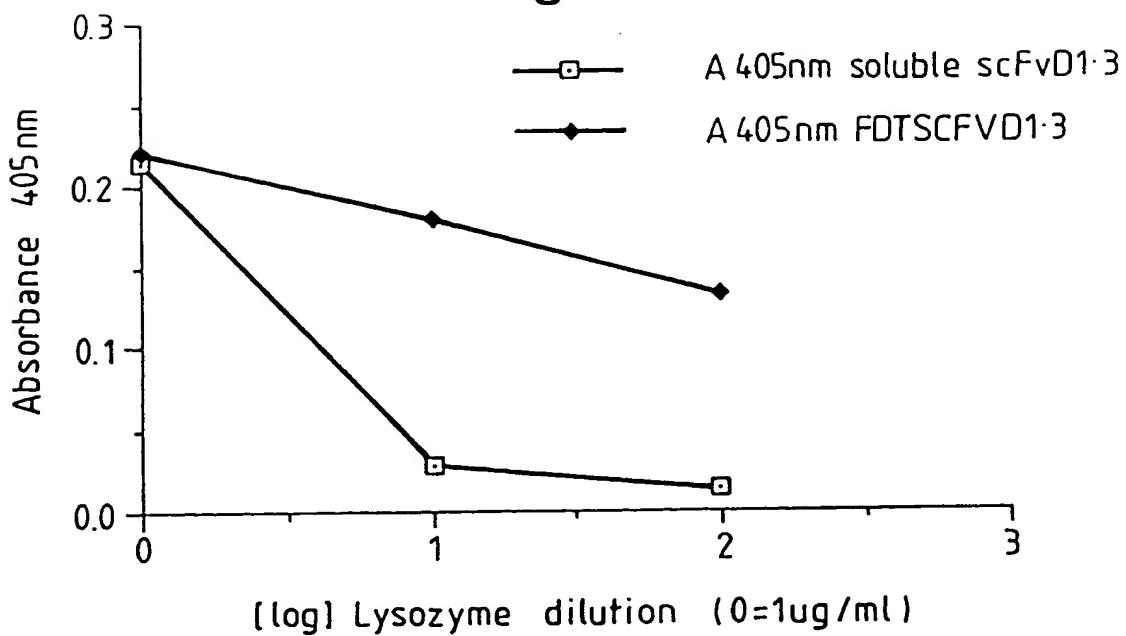




Fig.32.

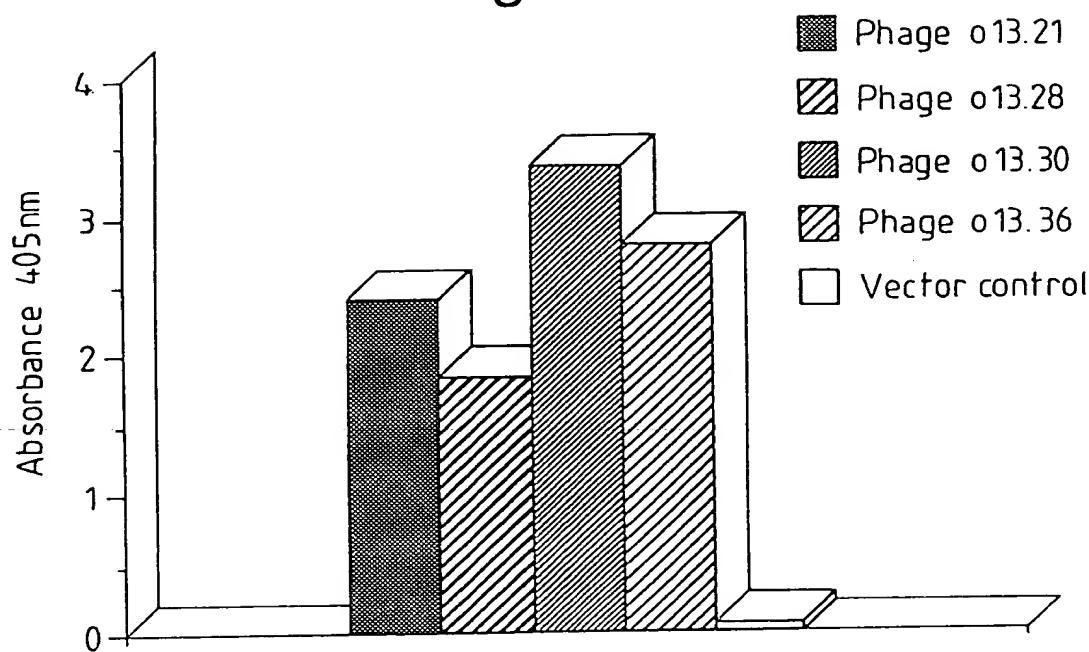


Fig.33.

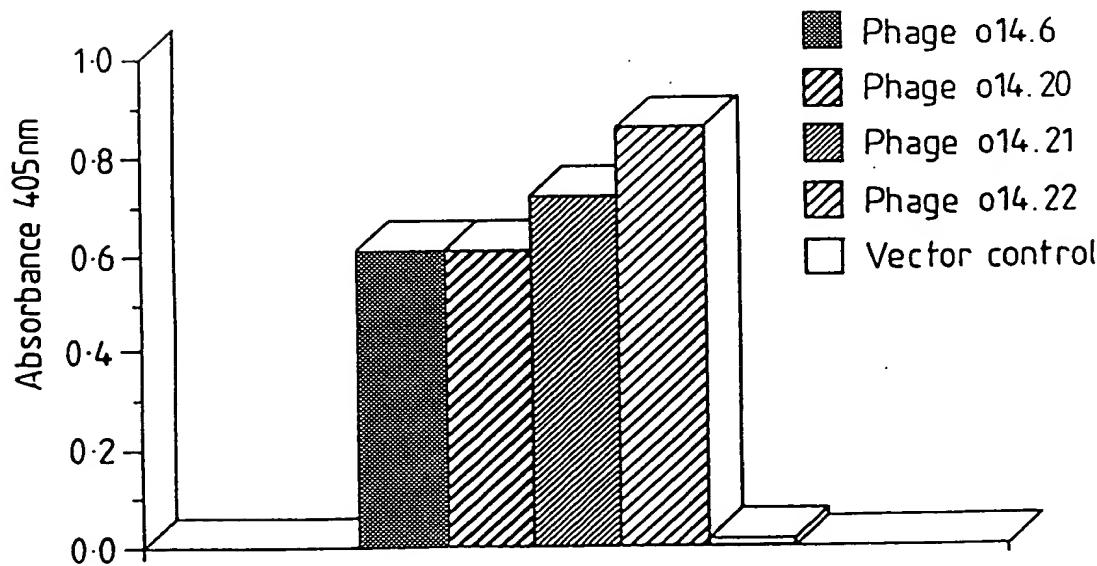




Fig.34.

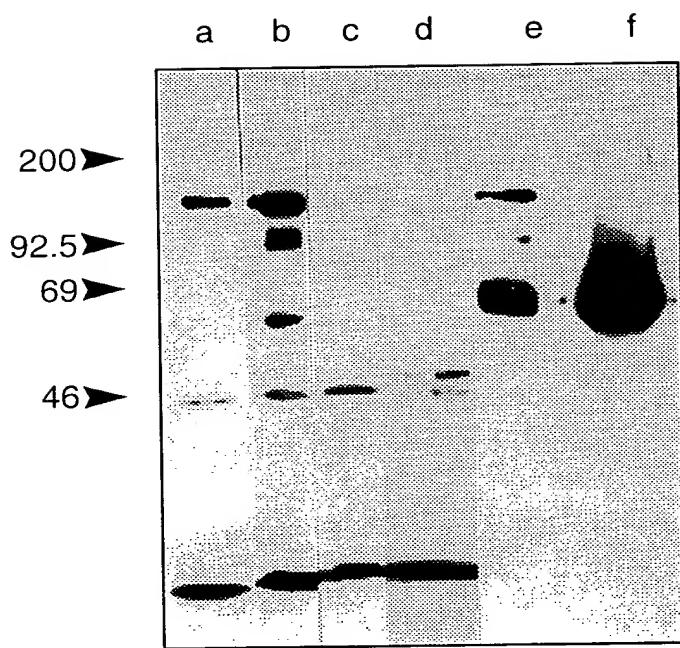




Fig.35A.

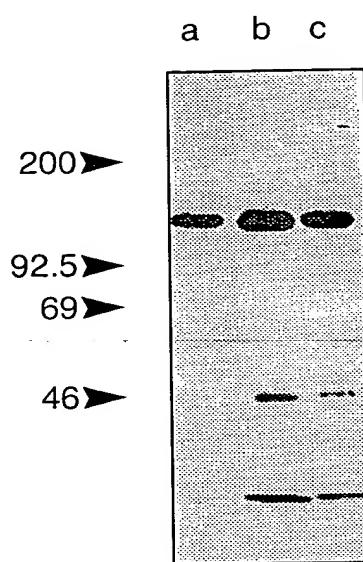


Fig.35B.

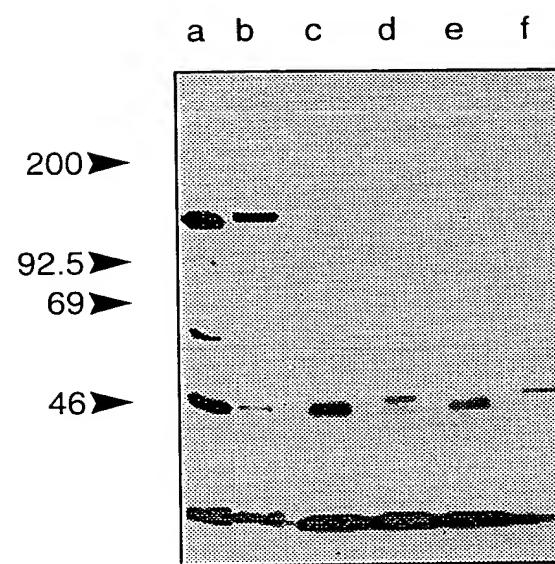


Fig.36.

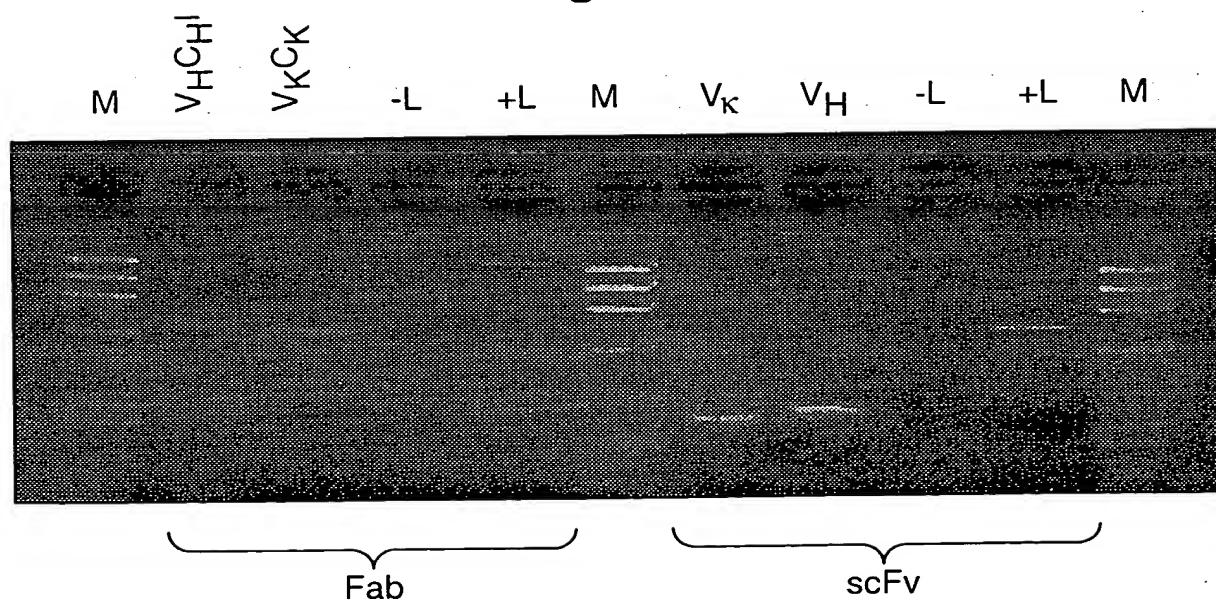




Fig.37.

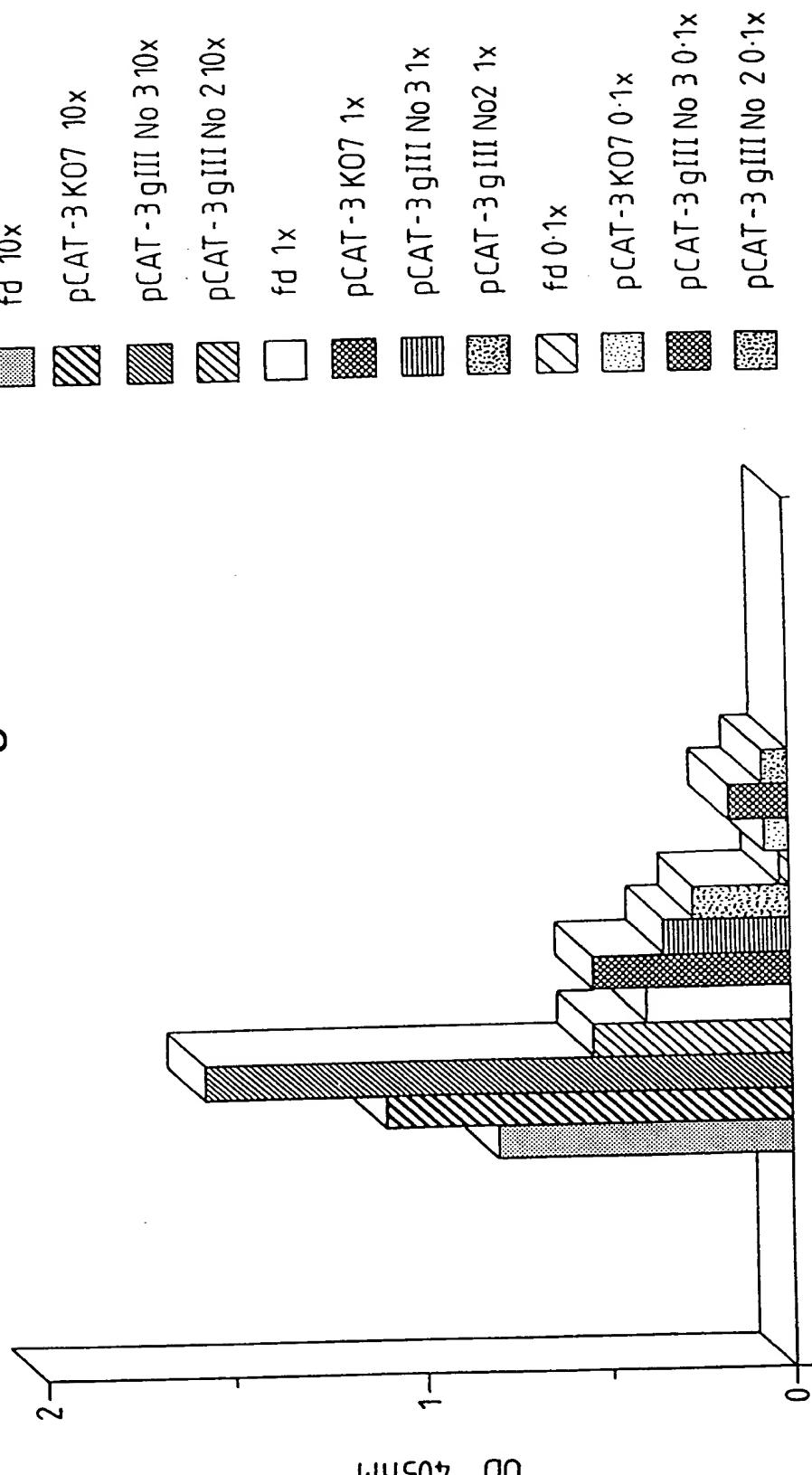




Fig.38A.

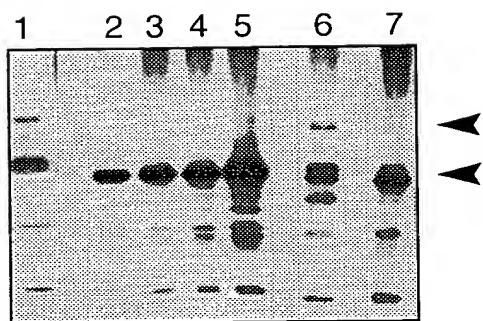


Fig.38B.

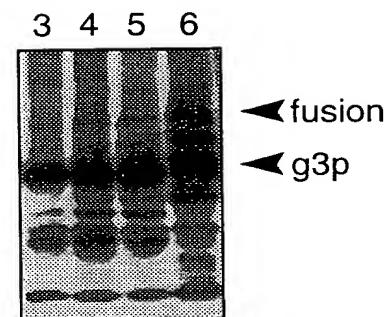




Fig.39.

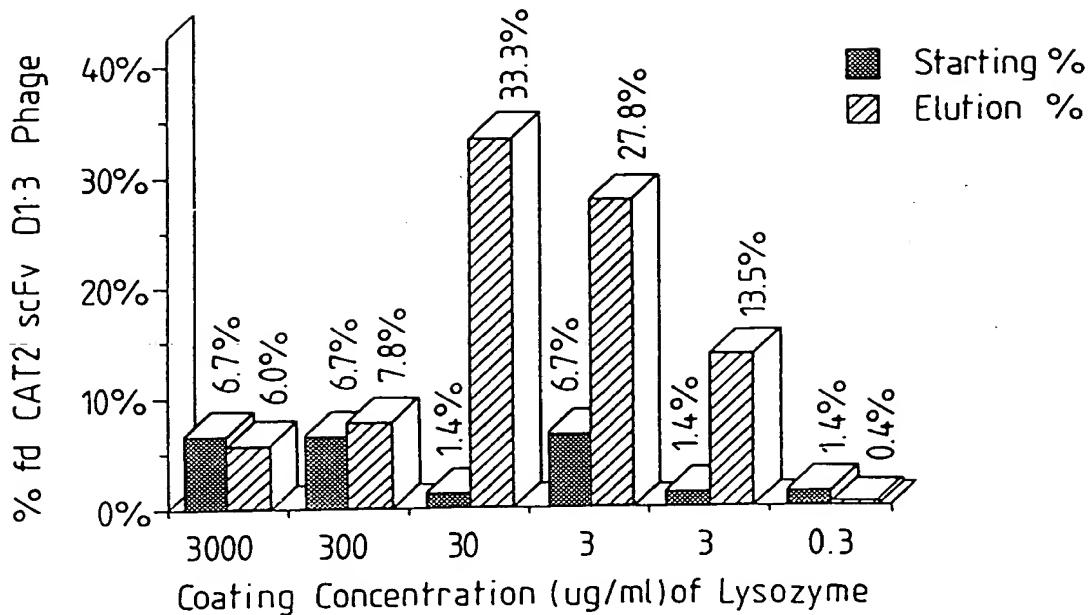


Fig.40.

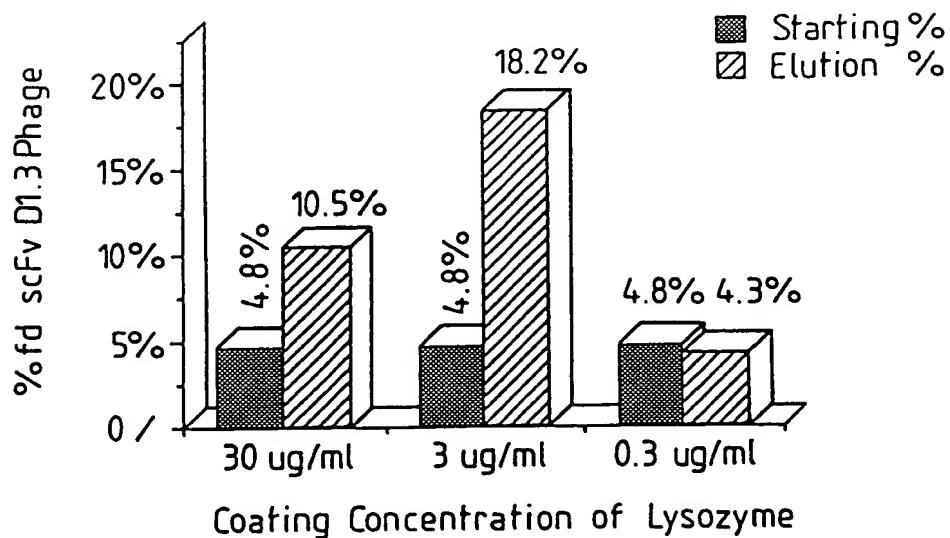




Fig.41.

1 2

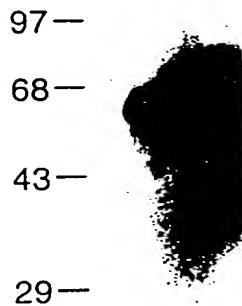


Fig.42.

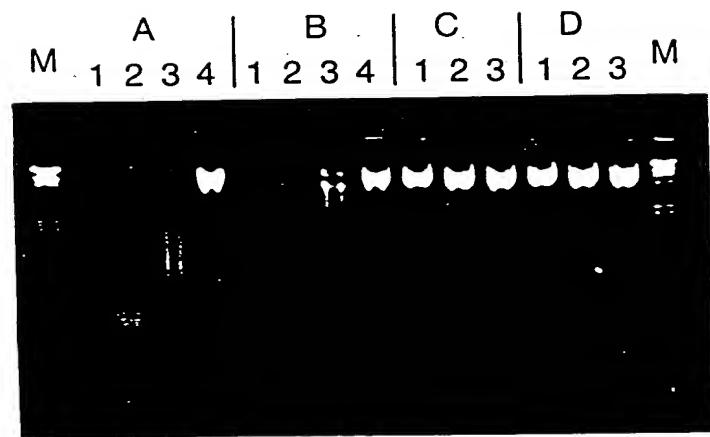




Fig.43.

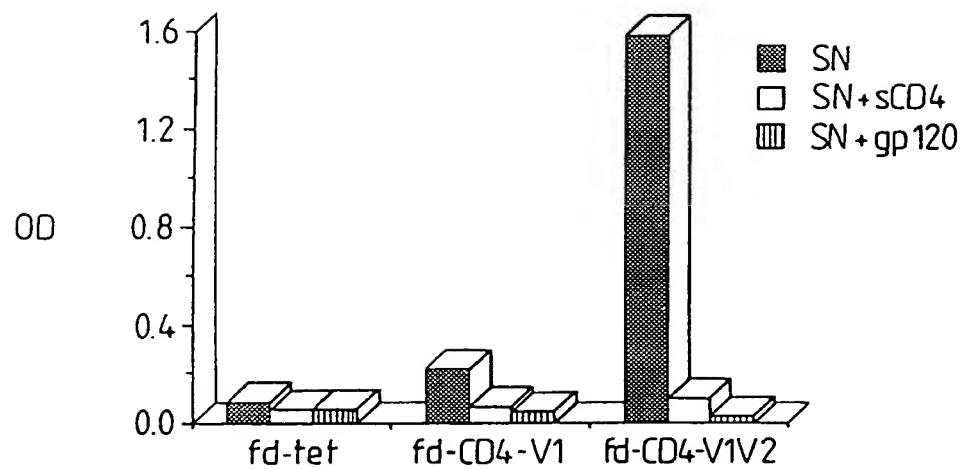




Fig. 44a



Fig. 44 b



Fig.45.

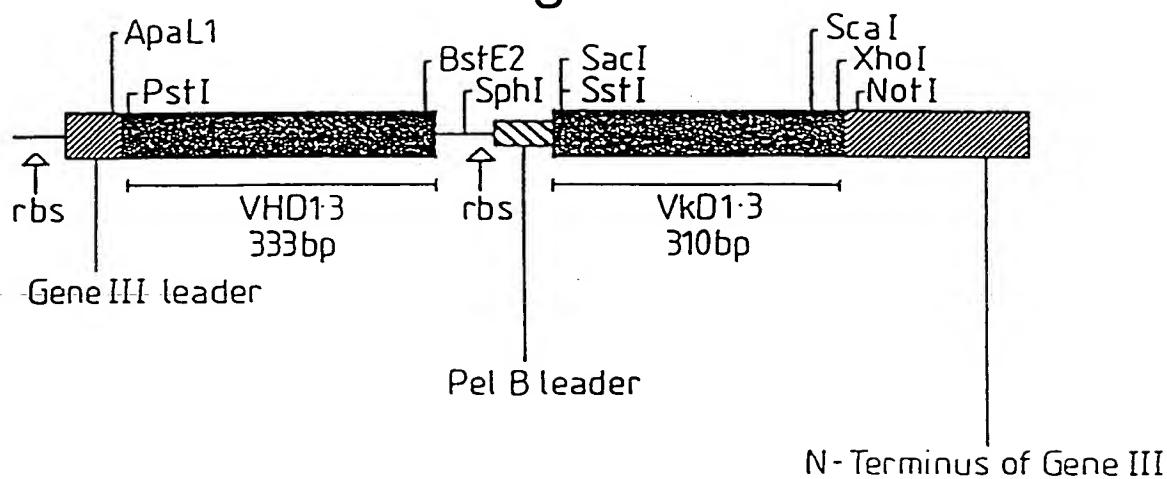


Fig.46.

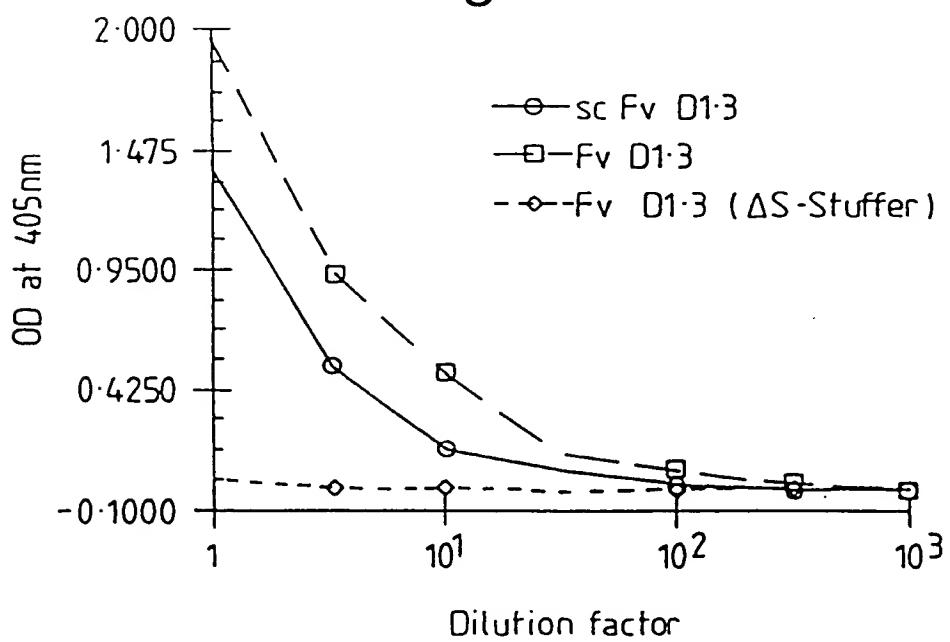




Fig.47.

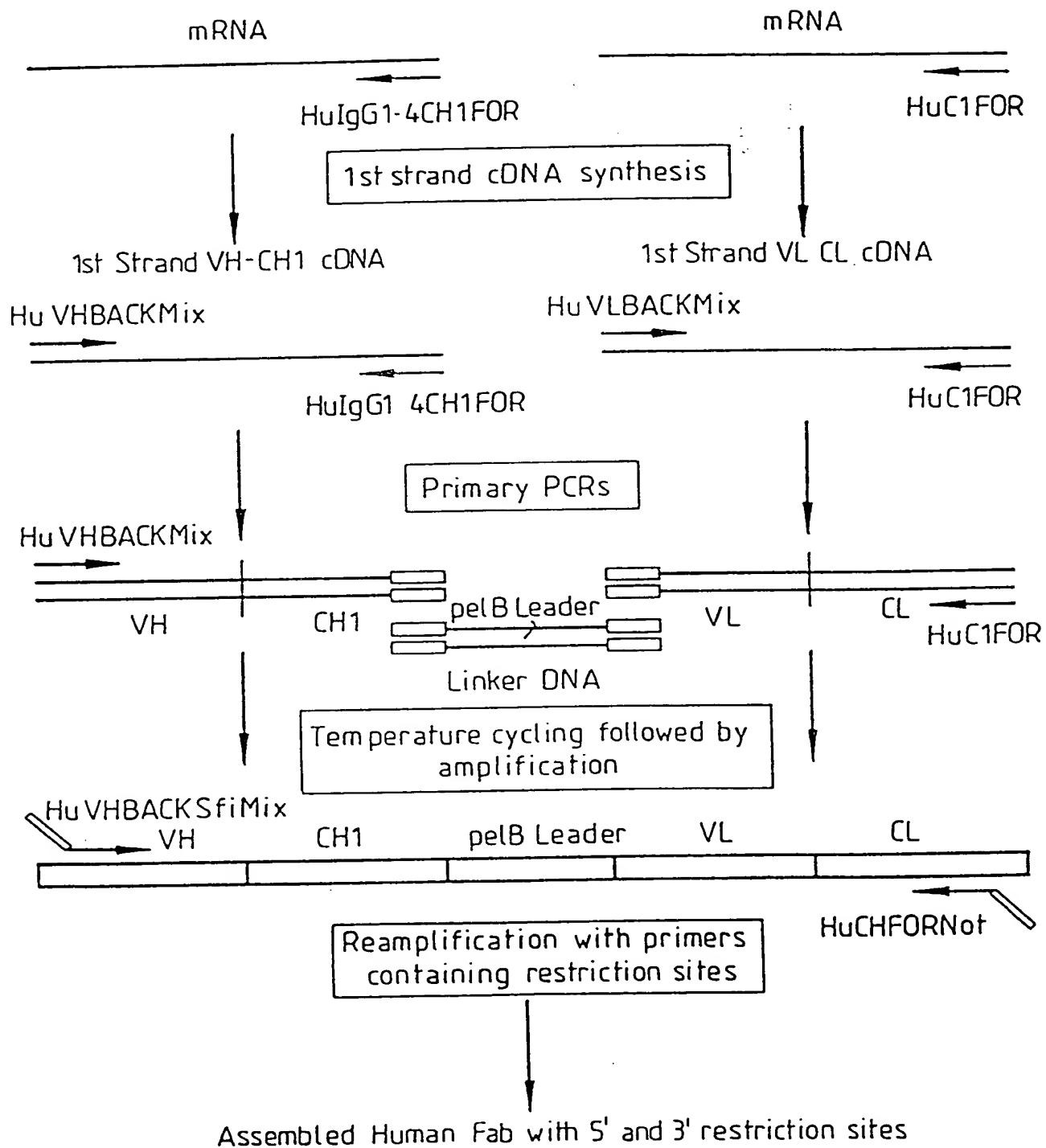




Fig. 48a

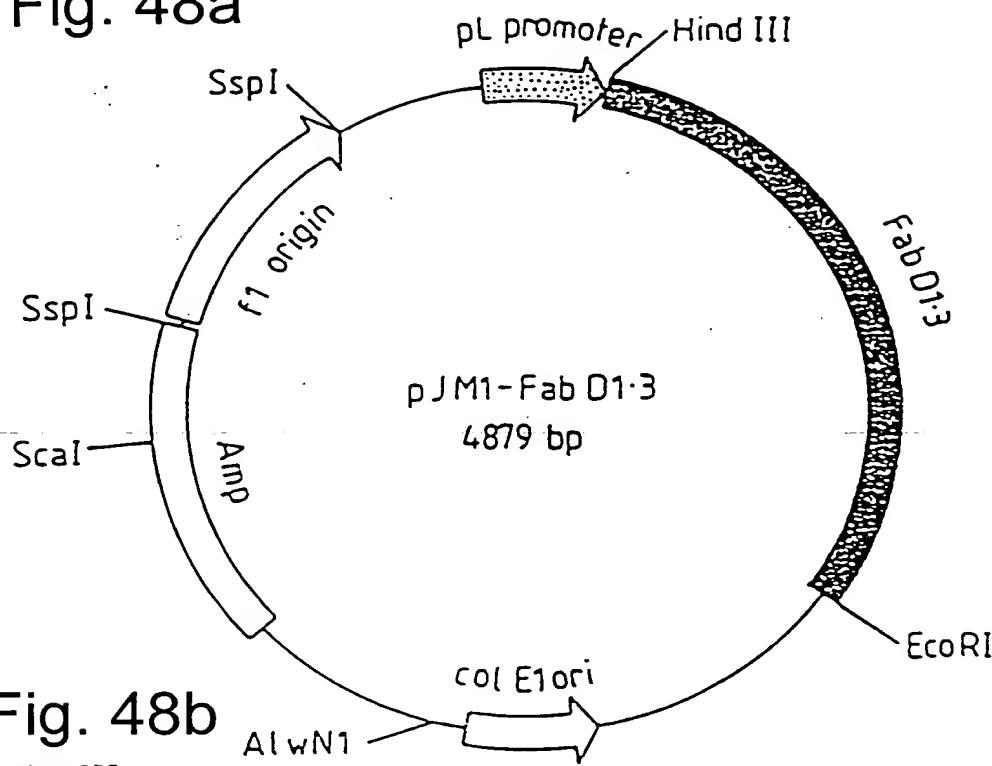


Fig. 48b

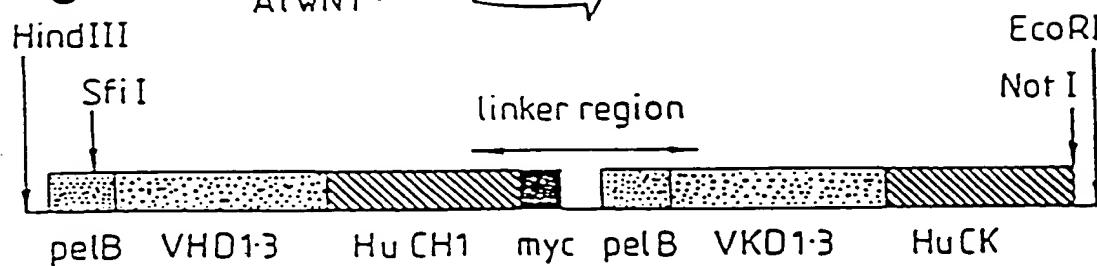


Fig. 48c

← 3' Human CH1 and hinge →
 K P S N T K V D K K V E P K S S T K T H T
 AACCCCCAGCAACACCAAGGTGGACAACAAAGTTGAGGCCAAATCTTCAACTAAGACCCACACA

← myc peptide tag →
 S G G E Q K L I S E E D L N * * (SEQ ID NO. 263)
 TCAGGAGGTGAACAGAACAGCTCATCTCAGAAGAGGATCTGAATTATAAGGGACCTTCATGCA

← pelB leader →
 M K Y L L P T A A A G L
 AATTCATTTCAAGGAGACAGTCATAATGAAATACTTATGCTACGGCAGCGCGCTGGATTTG

← 5' Vk →
 L L P A A Q P A M A D I E L T Q S P (SEQ ID NO. 264)
 TATTACCTGCTGCCAACCAACCAGGATGGGGACATGGAGTTACACCCAGTCTCC (SEQ ID NO. 265)



Fig.49.

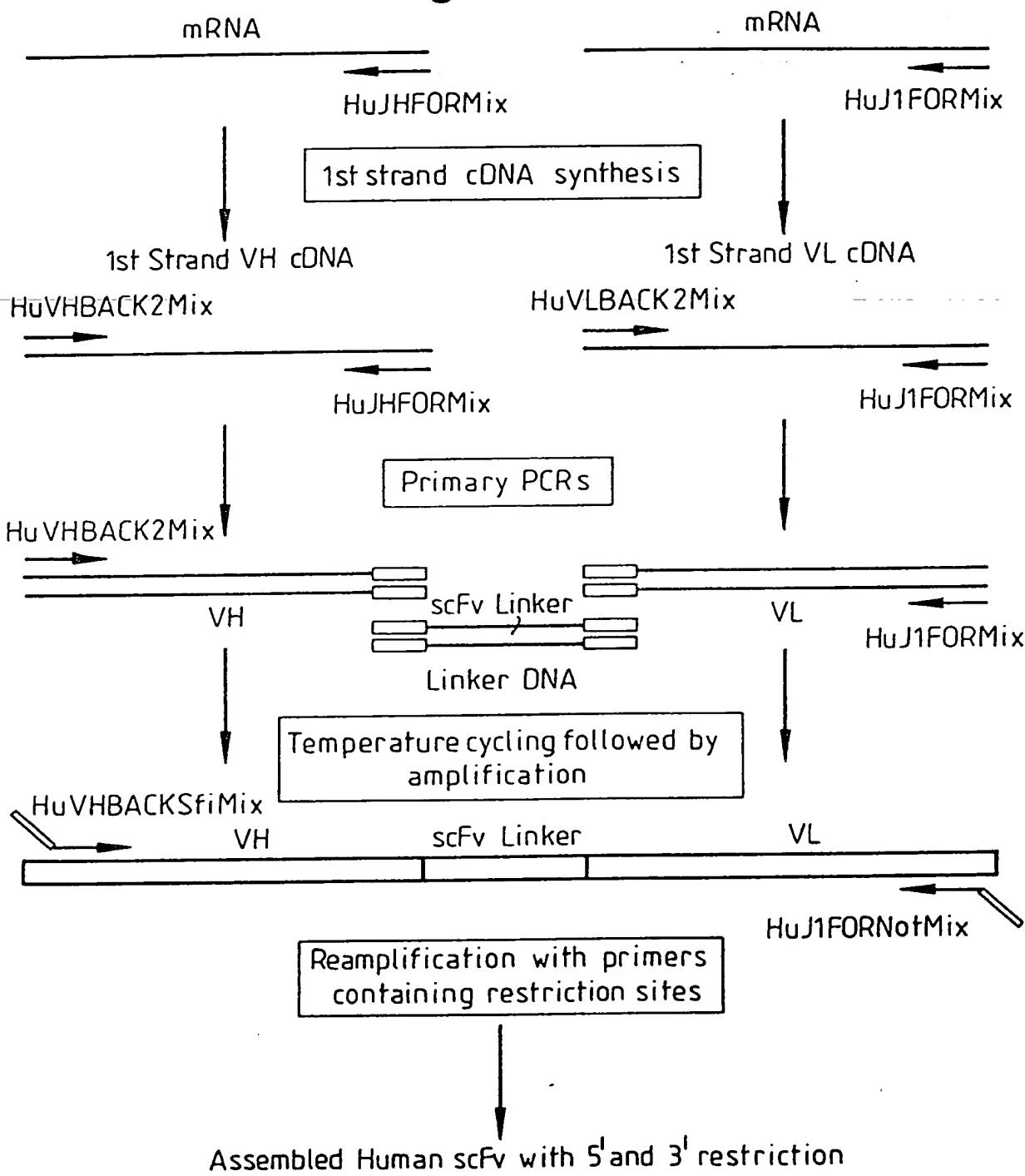




Fig.50a

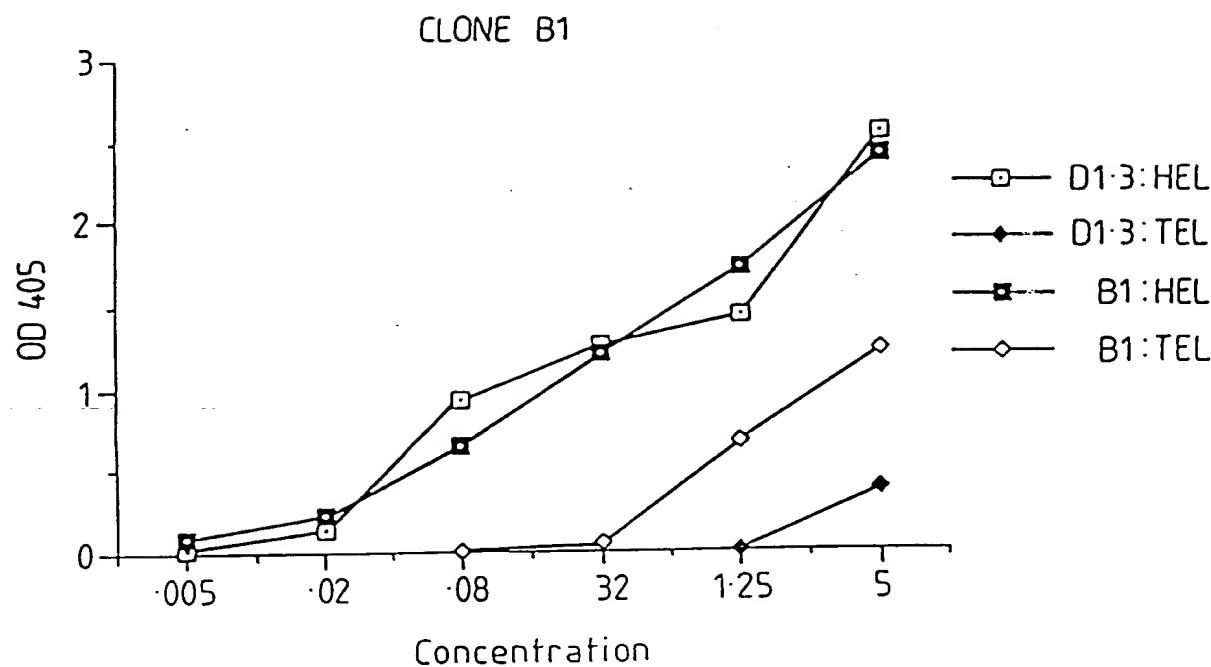


Fig.50b

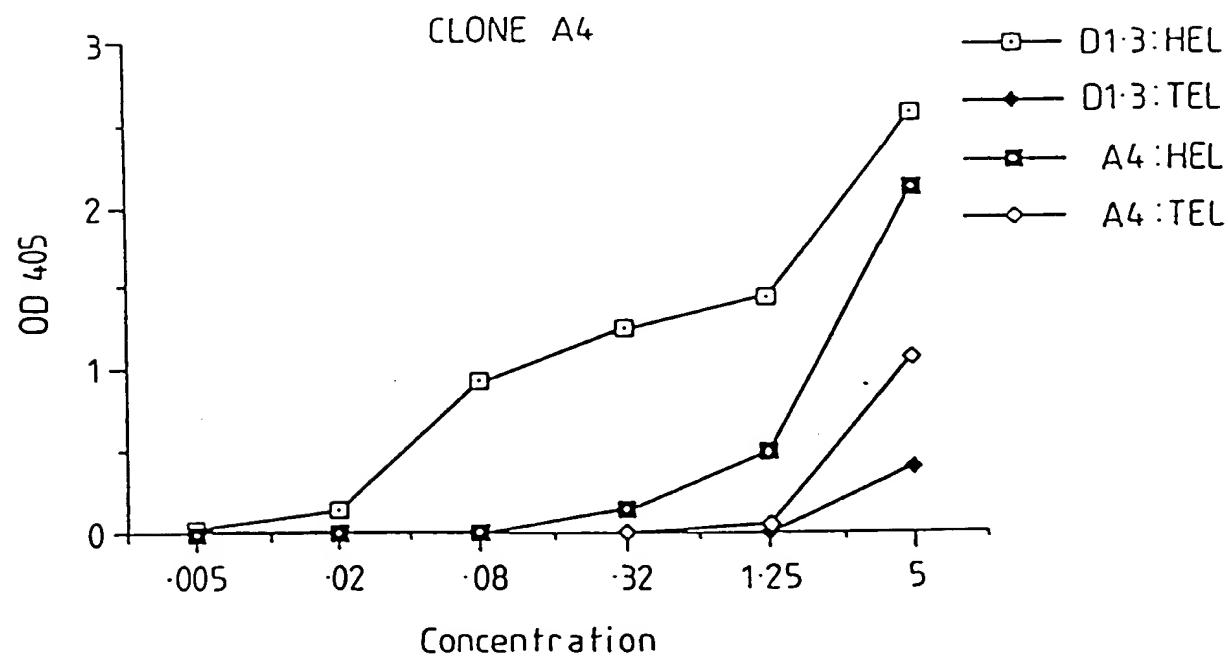




Fig.51.

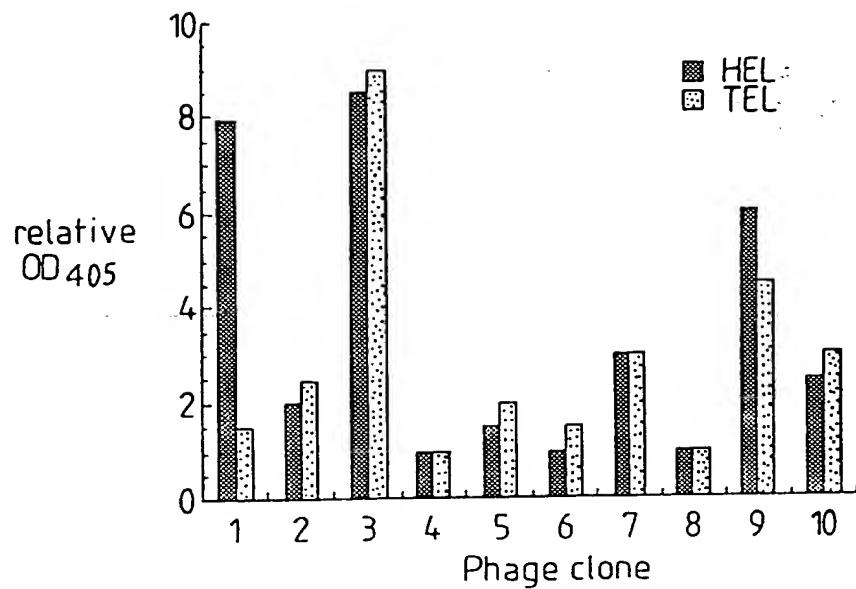


Fig.53.

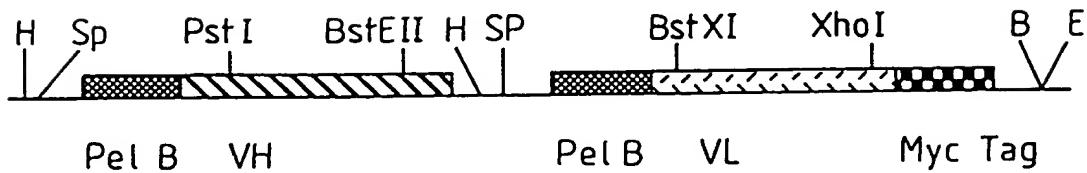




Fig.52.

CDR 1	CDR 2	CDR 3
D1 . 3 DIQMTQSPASLSASVGETVTITCRASNTHNYLA M1F DIELTQSPSSLSASLGERVSLTCRASQDIGSSLN M21 DIELTQSPALMAASPGEKVTITCSVSSSISSSNLHWYQQKSETSPKWIYGTSNLAS	WYQQKQGKSPQLLVYYTTTLAD WLQQEPDGTIKR LIYATSSLDS	GVPVRFSGSGSGTQYSLKINSLQPEDFGSYYCQHFWS GVPKRFSGSRSGSDYSLTISSLESED GVPVRFSGSGSGTYSLTISSMEAEDAATYYCQQWSSYPLT